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(54) Title: GENE EXPRESSION PROFILES IN NORMAL AND CANCER CELLS (57) Abstract As a step towards understanding the complex differences between normal and cancer cells, gene expression patterns were examined in gastrointestinal tumors. More than 300,000 transcripts derived from at least 45,000 different genes were analyzed. Although extensive similarity was noted between the expression profiles, more than 500 transcripts that were expressed at significantly different levels in normal and neoplastic cells were identified. These data provide insights into the extent of expression differences underlying malignancy and reveal genes that are useful as diagnostic or prognostic markers.		

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Gene Expression Profiles in Normal and Cancer Cells

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TECHNICAL FIELD OF THE INVENTION

This invention is related to the diagnosis of cancer, and tools for carrying out such diagnosis.

BACKGROUND OF THE INVENTION

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Much of cancer research over the past 50 years has been devoted to the analyses of genes that are expressed differently in tumor cells compared to their normal counterparts. Although hundreds of studies have pointed out differences in the expression of one or a few genes, no comprehensive study of gene expression in the cancer cell has been reported. It is therefore not known how many genes are expressed differentially in tumor versus normal cells, whether the bulk of these differences are cell autonomous rather than being dependent on the tumor microenvironment, and whether most differences are cell-type specific or tumor specific. Thus there is a need in the art for information on the molecular changes that occur in cells during cancer development and progression.

SUMMARY OF THE INVENTION

According to one embodiment of the invention, a method is provided for diagnosing colon cancer in a sample suspected of being neoplastic. The method comprises the steps of:

5 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 3;

10 identifying the first sample as neoplastic when the level of the at least one transcript is found to be lower in the first sample than in the second sample.

According to another embodiment of the invention, another method is provided for diagnosing colon cancer in a sample suspected of being neoplastic. The method comprises the steps of:

15 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2;

20 identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

25 In another embodiment of the invention an isolated and purified human nucleic acid molecule is provided. The molecule comprises a SAGE tag selected from SEQ ID NO:1-732.

30 In yet another aspect of the invention an isolated nucleotide probe is provided. The probe comprises at least 12 nucleotides of a human nucleic acid molecule, wherein the human nucleic acid molecule comprises a SAGE tag selected from SEQ ID NO: 1-732.

According to another aspect of the invention a method is provided for diagnosing pancreatic cancer in a sample suspected of being neoplastic. The method comprises the steps of:

5 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a pancreatic tissue suspected of being neoplastic and the second sample is of a normal human colon tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4;

10 identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

According to still another embodiment of the invention a method of diagnosing cancer in a sample suspected of being neoplastic is provided. The method comprises the steps of:

15 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a tissue suspected of being neoplastic and the second sample is of a normal human tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5;

20 identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

25 According to another embodiment of the invention a method is provided to aid in the determination of a prognosis for a colon cancer patient. The method comprises the steps of:

30 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic colonic tissue and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 3;

determining a poorer prognosis if the level of the at least one transcript is found to be lower in the first sample than in the second sample.

According to another aspect of the invention a method to aid in determining a prognosis for a patient with colon cancer is provided. The method comprises the steps of:

comparing the level of at least one transcript in a first tissue sample to a second sample, wherein the first sample is of a colonic cancer tissue and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2;

determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

In yet another embodiment of the invention a method is provided for diagnosing colon cancer in a sample suspected of being neoplastic. The method comprises the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 3;

identifying the first sample as neoplastic when the level of expression of the protein is found to be lower in the first sample than in the second sample.

In another aspect of the invention a method of diagnosing colon cancer in a sample suspected of being neoplastic is provided. The method comprises the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript

identified by a tag selected from the group consisting of those shown in Table 2;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

5 According to another embodiment of the invention a method is provided to aid in determining a prognosis of a patient having pancreatic cancer. The method comprises the steps of:

10 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic pancreatic tissue and the second sample is of a normal human colon tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4;

 determining a poorer prognosis if transcription is found to be higher in the first sample than in the second sample.

15 In yet another aspect of the invention a method to aid in providing a prognosis for a cancer patient is provided. The method comprises the steps of:

20 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic tissue and the second sample is of a normal human tissue of the same tissue type, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5;

 determining a poorer prognosis if transcription is found to be higher in the first sample than in the second sample.

25 According to still another aspect of the invention, a method is provided for diagnosing pancreatic cancer in a sample suspected of being neoplastic. The method comprises the steps of:

30 comparing the level of expression of at least one protein encoded by a transcript in a first sample of a tissue to a second sample, wherein the first sample is of a pancreatic tissue suspected of being neoplastic and the second sample is of a normal human colon tissue, wherein said protein is

encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

5 According to yet another aspect of the invention a method is provided for diagnosing cancer in a sample suspected of being neoplastic. The method comprises the steps of:

10 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a tissue suspected of being neoplastic and the second sample is of a normal human tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

15 In still another embodiment of the invention a method is provided to aid in the determination of a prognosis of a colon cancer patient. The method comprises the steps of:

20 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic colonic tissue and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 3;

determining a poorer prognosis if the level of expression is found to be lower in the first sample than in the second sample.

25 In still another embodiment of the invention a method is provided to aid in determining a prognosis for a patient with colon cancer. The method comprises the steps of:

30 comparing the level of expression of at least one protein in a first tissue sample to a second sample, wherein the first sample is of a colonic cancer tissue and the second sample is of a normal human colonic tissue, and

wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2;

determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

5 In still another aspect of the invention a method is provided to aid in determining a prognosis of a patient having pancreatic cancer. The method comprises the steps of:

10 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic pancreatic tissue and the second sample is of a normal human colon tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4;

determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

15 According to even a further aspect of the invention a method is provided to aid in providing a prognosis for a cancer patient. The method comprises the steps of:

20 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic tissue and the second sample is of a normal human tissue of the same tissue type, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5;

determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

25 In still another embodiment of the invention a method of treating a cancer cell is provided. The method comprises the step of:

30 administering to a cancer cell an antibody which specifically binds to a protein encoded by a transcript identified by a tag selected from the group consisting of those shown in Tables 2, 4, and 5, wherein the antibody is linked to a cytotoxic agent.

In another aspect of the invention an antibody linked to a cytotoxic agent is provided. The antibody specifically binds to a protein encoded by a transcript identified by a tag selected from the group consisting of those shown in Tables 2, 4, and 5.

5 According to another aspect of the invention, a method of detecting colon cancer in a patient is provided. The method comprises the steps of:

comparing the level of at least one protein or transcript in a first body sample to a second body sample, wherein the first sample is a body sample of the patient and the second sample is of a normal human, wherein the protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

10 identifying neoplasia when the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

15 In another aspect of the invention a method of detecting pancreatic cancer in a patient is provided. The method comprises the steps of:

comparing the level of at least one protein or transcript encoded by a transcript in a first sample of a tissue to a second sample, wherein the first sample is of the patient and the second sample is of a normal human, wherein said protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown Table 4, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

20 identifying neoplasia when the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

Also provided by the present invention is a method of detecting cancer in a patient. The method comprises the steps of:

30 comparing the level of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of patient and the second sample is of a normal human, wherein said protein is encoded by a

transcript and the transcript is identified by a tag selected from the group consisting of those shown Table 5, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

5 identifying neoplasia when the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

Additionally provided by the present invention is a method to aid in the determination of a prognosis for a colon cancer patient. The method comprises the steps of:

10 comparing the level of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of a colon cancer patient and the second sample is of a normal human, wherein the protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown in Table 3, wherein the first and second body sample
15 is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one protein or transcript is found to be lower in the first sample than in the second sample.

20 Provided by another embodiment of the invention is a method to aid in determining a prognosis for a patient with colon cancer. The method comprises the steps of:

comparing the level of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of a colonic cancer patient and the second sample is of a normal human, wherein the protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second
25 sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

5 According to still another aspect of the invention, a method to aid in determining a prognosis of a patient having pancreatic cancer is provided. The method comprises the steps of:

10 comparing the level of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of a pancreatic cancer patient and the second sample is of a normal human, wherein said protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown Table 4, wherein said first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

15 determining a poorer prognosis if the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

Also provided by the present invention is a method to aid in providing a prognosis for a cancer patient. The method comprises the steps of:

20 comparing the level of expression of at least one protein or transcript in a first sample to a second sample, wherein the first sample is of a cancer patient and the second sample is of a normal human, wherein said protein is encoded by a transcript and the transcript is identified by a tag selected from the group consisting of those shown Table 5, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

25 determining a poorer prognosis if the level of the at least one protein or transcript is found to be higher in the first sample than in the second sample.

30 The present invention further includes antisense oligonucleotides complementary in whole or in part to SEQ ID NOS:1-732.

This invention also provides a method for screening for candidate agents that modulate the expression of a polynucleotide selected from the group consisting of the polynucleotides in SEQ ID NOS.1-732 or their respective complements, by contacting a test agent with a pancreatic or colon cell and monitoring expression of the polynucleotide, wherein the test agent which modifies the expression of the polynucleotide is a candidate agent.

The present invention provides the art with new methods and reagents for diagnosing and prognosing cancers. In addition, some of the newly disclosed genes may play an important role in the development of cancers.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1. Comparison of expression patterns in colorectal cancers and normal colon epithelium. **(FIG. 1A)** A semi-logarithmic plot reveals 51 tags that were decreased more than 10 fold in primary CR cancer cells whereas 32 tags were increased more than 10 fold. 62,168 and 60,878 tags derived from normal colon epithelium and primary CR cancers, respectively, were used for this analysis. The relative expression of each transcript was determined by dividing the number of tags observed in tumor and normal tissue as indicated. To avoid division by 0, a tag value of 1 was used for any tag that was not detectable in one of the samples. These ratios were then rounded to the nearest integer and their distribution plotted on the abscissa. The number of genes displaying each ratio was plotted on the ordinate. Tu: CR tumors; NC: Normal colon. **(FIG. 1B and FIG. 1C)** Differentially expressed genes in colorectal cancers. The number of transcripts found to be differentially expressed ($P < 0.01$) are presented as Venn diagrams. Diagrams of transcripts that were decreased **(FIG. 1B)** or increased **(FIG. 1C)** in CR cancers compared to normal colon epithelium. Comparisons were between primary tumors and cells in culture as indicated.

Fig. 2. Northern blot analysis of genes differentially expressed in gastrointestinal neoplasia. Northern blot analysis was performed on total RNA (5 μ g isolated from primary CR carcinomas (T) and matching normal colon epithelium (N), or pancreatic carcinomas. The top panel in each case show an

example of the ethidium bromide stained gels prior to transfer. The number of SAGE tags observed in the original analysis is indicated to the right of each blot. (FIG. 2A) Examples of transcripts that were decreased or increased in CR cancers. (FIG. 2B) Examples of transcripts increased in pancreatic cancers (10). (FIG. 2C) Examples of transcripts elevated in cancer which were or were not cancer type specific. Probes used for Northern blot analysis were as follows (Human SAGE Tag unique identifier, gene name, (GenBank accession number)): (FIG. 2A) H204104, Guanylin (M95714); H259108, (see Table 2); H1000193, (see Table 2); H998030, (see Table 2). (FIG. 2B) H294155, RIG-E (U42376); H560056, TIMP-1 (S68252). (FIG. 2C) H802810, EST338411 (W52120); H85882, 1-8D (X57351); H618841, GA733-1 (X13425).

Tables 2-5. Transcripts Differentially Expressed in Human Cancer.

Tag sequence represents the NlaIII site plus the adjacent 11 bp SAGE tag. Tag number indicates a SAGE UID (unique identifier). NC, TU, CL, PT, PC, refers to the number of the indicated tag observed in RNA isolated from normal colorectal epithelium, primary colorectal cancers, colorectal cancer cell lines, primary pancreatic cancers, or pancreatic cancer cell lines, respectively. The Accession and Gene Name refer to representative GenBank entries that contain the tag sequence.

Table 2 Transcripts increased in colorectal cancer.

Table 3 Transcripts decreased in colorectal cancer.

Table 4 Transcripts increased in pancreatic cancer.

Table 5 Transcripts increased in pancreatic and colorectal cancer.

DETAILED DESCRIPTION

The inventors have discovered sets of human genes which are either upregulated or downregulated in cancer cells, as compared to normal cells. Specifically, certain genes have been found to be upregulated or downregulated in colorectal and/or pancreatic cancer cells, when compared to normal colon

cells. These sets of differentially regulated genes can be used as diagnostic markers, either individually or in sets of, for example, 2, 5, 10, 20, or 30.

Genes whose expression was detected to be increased in colorectal cancer are shown in Table 2. Genes whose expression was detected to be decreased in colorectal cancer are shown in Table 3. Genes whose expression was detected as increased in pancreatic cancer are shown in Table 4. Genes whose expression was detected as increased in both pancreatic cancer and colorectal cancer are shown in Table 5. These latter genes likely play a role in neoplastic development generally.

Tag sequences, as provided herein, uniquely identify genes. This is due to their length, and their specific location (3') in a gene from which they are drawn. The full length genes can be identified by matching the tag to a gene data base member, or by using the tag sequences as probes to physically isolate previously unidentified genes from cDNA libraries. The methods by which genes are isolated from libraries using DNA probes are well known in the art. See, for example, Veculescu et al., *Science* 270: 484 (1995), and Sambrook et al. (1989), *MOLECULAR CLONING: A LABORATORY MANUAL*, 2nd ed. (Cold Spring Harbor Press, Cold Spring Harbor, New York). Once a gene or transcript has been identified, either by matching to a data base entry, or by physically hybridizing to a cDNA molecule, the position of the hybridizing or matching region in the transcript can be determined. If the tag sequence is not in the 3' end, immediately adjacent to the restriction enzyme used to generate the SAGE tags, then a spurious match may have been made. Confirmation of the identity of a SAGE tag can be made by comparing transcription levels of the tag to that of the identified gene in certain cell types.

In addition to the sequences shown in SEQ ID NOS: 1-732, or their complements, this invention also provides the anti-sense polynucleotide stand, e.g. antisense RNA to these sequences or their complements. One can obtain an antisense RNA using the sequences provided in SEQ ID NOS: 1-732 and the methodology described in Vander Krol et al. (1988) *BioTechniques* 6:958.

The invention also encompasses polynucleotides which differ from that of the polynucleotides described above, but which produce the same phenotypic effect, such as the allele. These altered, but phenotypically equivalent polynucleotides are referred to "equivalent nucleic acids." This invention also encompasses polynucleotides characterized by changes in non-coding regions that do not alter the phenotype of the polypeptide produced therefrom when compared to the polynucleotide herein. This invention further encompasses polynucleotides, which hybridize to the polynucleotides of the subject invention under conditions of moderate or high stringency.

The polynucleotides can be conjugated to a detectable marker, e.g., an enzymatic label or a radioisotope for detection of nucleic acid and/or expression of the gene in a cell. A wide variety of appropriate detectable markers are known in the art, including fluorescent, radioactive, enzymatic or other ligands, such as avidin/biotin, which are capable of giving a detectable signal. In preferred embodiments, one will likely desire to employ a fluorescent label or an enzyme tag, such as urease, alkaline phosphatase or peroxidase, instead of radioactive or other environmental undesirable reagents. In the case of enzyme tags, colorimetric indicator substrates are known which can be employed to provide a means visible to the human eye or spectrophotometrically, to identify specific hybridization with complementary nucleic acid-containing samples. Briefly, this invention further provides a method for detecting a single-stranded polynucleotide identified by SEQ ID NOS.1-732 or its complement, by contacting target single-stranded polynucleotides with a labeled, single-stranded polynucleotide (a probe) which is at least 10 nucleotides of the complement of SEQ ID NOS: 1-732 (or the corresponding complement) under conditions permitting hybridization (preferably moderately stringent hybridization conditions) of complementary single-stranded polynucleotides, or more preferably, under highly stringent hybridization conditions. Hybridized polynucleotide pairs are separated from un-hybridized, single-stranded polynucleotides. The hybridized polynucleotide

pairs are detected using methods well known to those of skill in the art and set forth, for example, in Sambrook et al. (1989) *supra*.

The polynucleotides of this invention can be isolated using the technique described in the experimental section or replicated using PCR. The PCR technology is the subject matter of United States Patent Nos. 4,683,195, 4,800,159, 4,754,065, and 4,683,202 and described in PCR: The Polymerase Chain Reaction (Mullis et al. eds, Birkhauser Press, Boston (1994)) or MacPherson et al. (1991) and (1994), *supra*, and references cited therein. Alternatively, one of skill in the art can use the sequences provided herein and a commercial DNA synthesizer to replicate the DNA. Accordingly, this invention also provides a process for obtaining the polynucleotides of this invention by providing the linear sequence of the polynucleotide, nucleotides, appropriate primer molecules, chemicals such as enzymes and instructions for their replication and chemically replicating or linking the nucleotides in the proper orientation to obtain the polynucleotides. In a separate embodiment, these polynucleotides are further isolated. Still further, one of skill in the art can insert the polynucleotide into a suitable replication vector and insert the vector into a suitable host cell (procaryotic or eucaryotic) for replication and amplification. The DNA so amplified can be isolated from the cell by methods well known to those of skill in the art. A process for obtaining polynucleotides by this method is further provided herein as well as the polynucleotides so obtained.

RNA can be obtained by first inserting a DNA polynucleotide into a suitable host cell. The DNA can be inserted by any appropriate method, e.g., by the use of an appropriate gene delivery vector or by electroporation. When the cell replicates and the DNA is transcribed into RNA; the RNA can then be isolated using methods well known to those of skill in the art, for example, as set forth in Sambrook et al. (1989) *supra*. For instance, mRNA can be isolated using various lytic enzymes or chemical solutions according to the procedures set forth in Sambrook et al. (1989), *supra* or extracted by nucleic-acid-binding resins following the accompanying instructions provided by manufactures.

Polynucleotides having at least 10 nucleotides and exhibiting sequence complementarity or homology to SEQ ID NOS: 1-732 find utility as hybridization probes. In some aspects, the full coding sequence of the transcript, i.e., for SEQ ID NOS: 1-732, are known. Accordingly, any portion of the known sequences available in GenBank, or homologous sequences, can be used in the methods of this invention.

It is known in the art that a "perfectly matched" probe is not needed for a specific hybridization. Minor changes in probe sequence achieved by substitution, deletion or insertion of a small number of bases do not affect the hybridization specificity. In general, as much as 20% base-pair mismatch (when optimally aligned) can be tolerated. Preferably, a probe useful for detecting the aforementioned mRNA is at least about 80% identical to the homologous region of comparable size contained in the previously identified sequences identified by SEQ ID NOS:1-732, which correspond to previously characterized genes or SEQ ID NOS:1-732, which correspond to known ESTs. More preferably, the probe is 85% identical to the corresponding gene sequence after alignment of the homologous region; even more preferably, it exhibits 90% identity.

These probes can be used in radioassays (e.g. Southern and Northern blot analysis) to detect, prognose, diagnose or monitor various pancreatic or colon cells or tissue containing these cells. The probes also can be attached to a solid support or an array such as a chip for use in high throughput screening assays for the detection of expression of the gene corresponding to one or more polynucleotide(s) of this invention. Accordingly, this invention also provides at least one of the transcripts identified as SEQ ID NOS:1-732, or its complement, attached to a solid support for use in high throughput screens.

The total size of fragment, as well as the size of the complementary stretches, will depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the complementary region may be varied,

such as between about 10 and about 100 nucleotides, or even full length according to the complementary sequences one wishes to detect.

5 Nucleotide probes having complementary sequences over stretches greater than 10 nucleotides in length are generally preferred, so as to increase stability and selectivity of the hybrid, and thereby improving the specificity of particular hybrid molecules obtained. More preferably, one can design polynucleotides having gene-complementary stretches of more than 50 nucleotides in length, or even longer where desired. Such fragments may be readily prepared by, for example, directly synthesizing the fragment by
10 chemical means, by application of nucleic acid reproduction technology, such as the PCR technology with two priming oligonucleotides as described in U.S. Pat. No. 4,603,102 or by introducing selected sequences into recombinant vectors for recombinant production. A preferred probe is about 50-75 or more preferably, 50-100, nucleotides in length.

15 The polynucleotides of the present invention can serve as primers for the detection of genes or gene transcripts that are expressed in pancreatic or colon cells. In this context, amplification means any method employing a primer-dependent polymerase capable of replicating a target sequence with reasonable fidelity. Amplification may be carried out by natural or recombinant
20 DNA-polymerases such as T7 DNA polymerase, Klenow fragment of E.coli DNA polymerase, and reverse transcriptase.

A preferred amplification method is PCR. However, PCR conditions used for each reaction are empirically determined. A number of parameters influence the success of a reaction. Among them are annealing temperature
25 and time, extension time, Mg^{2+} ATP concentration, pH, and the relative concentration of primers, templates, and deoxyribonucleotides. After amplification, the resulting DNA fragments can be detected by agarose gel electrophoresis followed by visualization with ethidium bromide staining and ultraviolet illumination.

30 The invention further provides the isolated polynucleotide operatively linked to a promoter of RNA transcription, as well as other regulatory

sequences for replication and/or transient or stable expression of the DNA or RNA. As used herein, the term "operatively linked" means positioned in such a manner that the promoter will direct transcription of RNA off the DNA molecule. Examples of such promoters are SP6, T4 and T7. In certain
5 embodiments, cell-specific promoters are used for cell-specific expression of the inserted polynucleotide. Vectors which contain a promoter or a promoter/enhancer, with termination codons and selectable marker sequences, as well as a cloning site into which an inserted piece of DNA can be operatively linked to that promoter are well known in the art and commercially available.
10 For general methodology and cloning strategies, see Gene Expression Technology (Goeddel ed., Academic Press, Inc. (1991)) and references cited therein and Vectors: Essential Data Series (Gacesa and Ramji, eds., John Wiley & Sons, N.Y. (1994)), which contains maps, functional properties, commercial suppliers and a reference to GenEMBL accession numbers for various suitable
15 vectors. Preferable, these vectors are capable of transcribing RNA in vitro or in vivo.

Fragment of the sequences shown in SEQ ID NOS:1-732 or their respective complements also are encompassed by this invention, preferably at least 10 nucleotides and more preferably having at least 18 nucleotides. Larger
20 polynucleotides, e.g., cDNA or genomic DNA, which hybridize under moderate or stringent conditions to the polynucleotide sequences shown in SEQ ID NOS:1-732, or their respective complements, also are encompassed by this invention.

In one embodiment, these fragments are polynucleotides that encode
25 polypeptides or proteins having diagnostic and therapeutic utilities as described herein as well as probes to identify transcripts of the protein which may or may not be present. These nucleic acid fragments can be prepared, for example, by restriction enzyme digestion of the polynucleotide of SEQ ID NOS:1-732, or their complements, and then labeled with a detectable marker. Alternatively,
30 random fragments can be generated using nick translation of the molecule. For

methodology for the preparation and labeling of such fragments, see Sambrook et al., (1989) *supra*.

Expression vectors containing these nucleic acids are useful to obtain host vector systems to produce proteins and polypeptides. It is implied that these expression vectors must be replicable in the host organisms either as episomes or as an integral part of the chromosomal DNA. Suitable expression vectors include viral vectors, including adenoviruses, adeno-associated viruses, retroviruses, cosmids, etc. Adenoviral vectors are particularly useful for introducing genes into tissues *in vivo* because of their high levels of expression and efficient transformation of cells both *in vitro* and *in vivo*. When a nucleic acid is inserted into a suitable host cell, e.g., a procaryotic or a eucaryotic cell and the host cell replicates, the protein can be recombinantly produced. Suitable host cells will depend on the vector and can include mammalian cells, animal cells, human cells, simian cells, insect cells, yeast cells, and bacterial cells constructed using well known methods. See Sambrook et al. (1989) *supra*. In addition to the use of viral vector for insertion of exogenous nucleic acid into cells, the nucleic acid can be inserted into the host cell by methods well known in the art such as transformation for bacterial cells; transfection using calcium phosphate precipitation for mammalian cells; or DEAE-dextran; electroporation; or microinjection. See Sambrook et al. (1989) *supra* for this methodology. Thus, this invention also provides a host cell, e.g. a mammalian cell, an animal cell (rat or mouse), a human cell, or a procaryotic cell such as a bacterial cell, containing a polynucleotide encoding a protein or polypeptide or antibody.

When the vectors are used for gene therapy *in vivo* or *ex vivo*, a pharmaceutically acceptable vector is preferred, such as a replication-incompetent retroviral or adenoviral vector. Pharmaceutically acceptable vectors containing the nucleic acids of this invention can be further modified for transient or stable expression of the inserted polynucleotide. As used herein, the term "pharmaceutically acceptable vector" includes, but is not limited to, a vector or delivery vehicle having the ability to selectively target

and introduce the nucleic acid into dividing cells. An example of such a vector is a "replication-incompetent" vector defined by its inability to produce viral proteins, precluding spread of the vector in the infected host cell. An example of a replication-incompetent retroviral vector is LNL6 (Miller, A.D. et al. (1989) BioTechniques 7:980-990). The methodology of using replication-incompetent retroviruses for retroviral-mediated gene transfer of gene markers is well established (Correll et al. (1989) PNAS USA 86:8912; Bordignon (1989) PNAS USA 86:8912-52; Culver, K. (1991) PNAS USA 88:3155; and Rill, D.R. (1991) Blood 79(10):2694-700. Clinical investigations have shown that there are few or no adverse effects associated with the viral vectors, see Anderson (1992) Science 256:808-13.

Compositions containing the polynucleotides of this invention, in isolated form or contained within a vector or host cell are further provided herein. When these compositions are to be used pharmaceutically, they are combined with a pharmaceutically acceptable carrier.

This invention further encompasses genes, either genomic or cDNA, which code for a polypeptide or protein in the cell of interest. The genes specifically hybridize under moderate or stringent conditions to a polynucleotide identified by SEQ ID NOS: 1-732 or their respective complements. The process of identification of larger fragment or the full-length coding sequence to which the partial sequence depicted in SEQ ID NOS:1-732 hybridizes preferably involves the use of the methods and reagents provided in this invention, either singularly or in combination.

Five methods are disclosed herein which allows one of skill in the art to isolate the gene or cDNA corresponding to the transcripts of the invention.

RACE-PCR Technique

One method to isolate the gene or cDNA which code for a polypeptide or protein and which corresponds to a transcript of this invention, involves the 5'-RACE-PCR technique. In this technique, the poly-A mRNA that contains the coding sequence of particular interest is first identified by hybridization to

a sequence disclosed herein and then reverse transcribed with a 3'-primer comprising the sequence disclosed herein. The newly synthesized cDNA strand is then tagged with an anchor primer of a known sequence, which preferably contains a convenient cloning restriction site attached at the 5'end. The tagged
5 cDNA is then amplified with the 3'-primer (or a nested primer sharing sequence homology to the internal sequences of the coding region) and the 5'-anchor primer. The amplification may be conducted under conditions of various levels of stringency to optimize the amplification specificity. 5'-RACE-PCR can be readily performed using commercial kits (available from, e.g., BRL Life
10 Technologies Inc, Clotech) according to the manufacturer's instructions.

Identification of known genes or ESTs

In addition, databases exist that reduce the complexity of ESTs by assembling contiguous EST sequences into tentative genes. For example,
15 TIGR has assembled human ESTs into a database called THC for tentative human consensus sequences. The THC database allows for a more definitive assignment compared to ESTs alone. Software programs exist (give examples) that allow for assembling ESTs into contiguous sequences from any organism.

Isolation of cDNAs from a library by probing with the SAGE transcript or tag

Alternatively, mRNA from a sample preparation was used to construct cDNA library in the ZAP Express vector following the procedure described in Velculescu et al. (1997) Science 270:484. The ZAP Express cDNA synthesis kit (Stratagene) was used accordingly to the manufacturer's protocol. Plates
25 containing 250 to 2000 plaques are hybridized as described in Rupert et al. (1988) Mol. Cell. Bio. 8:3104 to oligonucleotide probes with the same conditions previously described for standard probes except that the hybridization temperature is reduced to room temperature. Washes are performed in 6X standard-saline-citrate 0.1% SDS for 30 minutes at room
30 temperature. The probes are labeled with 32P-ATP through use of T4 polynucleotide kinase.

Table 2 - Transcripts increased in colon cancer
**Transcripts increased in only colon primary tumors
 compared to normal colon (61 genes)**

NC: Normal Colon

TU: Colon Primary Tumor

CL: Colon Cancer Cell Line

PT: Pancreatic Primary Tumor

PC: Pancreatic Cancer Cell Line

#	Tag Sequence	Tag Number	NC	TU	CL	PT	PC	Accession	Gene Name
1	CATGCACCTAATTGG	H285759	612	755	411	161	333	F15516	H.sapiens mitochondrial EST sequence (1-4-12) from
2	CATGTGATTTCACIT	H933704	452	595	235	80	314	U35430	Human cytochrome c oxidase subunit III (COIII) pse
3	CATGCCCTGTAATCCC	H388150	433	549	380	443	197	Z70701	H.sapiens mRNA (fetal brain cDNA c2.11).
								X71347	H.sapiens HNF1-C mRNA.
								X71346	H.sapiens HNF1-B mRNA.
4	CATGCACTACTCACC	H291282	293	527	78	14	83	U09500	Human mitochondrial cytochrome b gene, partial cds
5	CATGGTGAAACCCCA(G)	H753750	392	517	389	453	194	X66785	H.sapiens mRNA for transacylase (DBT).
								X17648	Human mRNA for granulocyte-macrophage colony-stimu
								U09087	Human thymopoietin beta mRNA, complete cds.
								U09088	Human thymopoietin gamma mRNA, complete cds.
								U20770	Human metastasis suppressor (KAI1) mRNA, complete
								W15552	zb91h11.s1 Soares parathyroid tumor NblHPA Homo sap
6	CATGGGCTTTAGGGA	H687915	37	372	6	29	11	W32091	zc05d03.s1 Soares parathyroid tumor NblHPA Homo sap
								R62866	yl11d07.r1 Homo sapiens cDNA clone 138925 5'.
								X89839	H.sapiens mitochondrial DNA for loop attachment se
7	CATGACTTTCCAAA	H130369	32	272	32	23	20	T11555	A1486F Homo sapiens cDNA clone A1486 similar to Mi
8	CATGTGGTGATGCA	H965434	53	271	6	30	5	T15773	IB1870 Homo sapiens cDNA 3'end similar to Human mi
9	CATGAGGGTGTTTC	H175872	26	218	7	20	10	X12544	Human mRNA for HLA class II DR-beta (HLA-DR B).
10	CATGAGGTCAGGAGA(T)	H177315	93	213	113	148	58	S73483	phosphorylase kinase catalytic subunit PHKG2 homol
								X74301	H.sapiens mRNA for MHC class II transactivator.
11	CATGTTGGCCAGGCT	H1025322	124	194	63	111	51	U28687	Human zinc finger containing protein ZNF157 (ZNF15
								U29119	Human leiomyoma LM-196.4 ectopic sequence from HMG
								U56236	Human Fc alpha receptor b mRNA, complete cds.
								W03751	za62h11.r1 Soares fetal liver spleen INFLS Homo sa
12	CATGATCAGCCCTC	H214616	97	186	17	41	49	W03770	za63f10.r1 Soares fetal liver spleen INFLS Homo sa

[illegible]

36	CATGGTGAAACCCA	H753749	9	31	22	30	4	T95857	ye42f01.s1 Homo sapiens cDNA clone 120409 3' simil
								W03237	za35b09.r1 Soares fetal liver spleen INFLS Homo sa
								W03326	za63g03.r1 Soares fetal liver spleen INFLS Homo sa
37	CATGGAAACTGAACA	H526210	6	26	17	5	3	X54195	Human line-1 element DNA, host sequence flanking t
								U29607	Human methionine aminopeptidase mRNA, complete cds
								H95100	yw57b10.r1 Homo sapiens cDNA clone 256315 5' simil
38	CATGACTTTTAAAA	H131009	1	22	4	1	0		Human keratinocyte cDNA, clone 067.
39	CATGGACTGCGTGCC	H555450	0	21	7	9	12	D29062	Human keratinocyte cDNA, clone 713.
								D29563	FB3B5 Homo sapiens cDNA clone FB3B5 3' end.
40	CATGTCAAGTGGTAGT	H863923	4	21	2	2	1	T03196	H.sapiens CpG DNA, clone 164a10, reverse read cpg1
41	CATGAAACTGTGTT	H7916	2	20	2	2	1	Z37093	H.sapiens CpG island DNA genomic MseI fragment, cl
								Z60184	H.sapiens CpG island DNA genomic MseI fragment, cl
								Z63649	H.sapiens CpG island DNA genomic MseI fragment, cl
								W31349	zb95d06.s1 Soares parathyroid tumor NbHPA Homo sap
42	CATGGGGGGGGGGT	H699051	0	19	0	0	0		zb96h101.s1 Soares parathyroid tumor NbHPA Homo sap
43	CATGGTGGCCGTGCC		2	19	1	0	0	W31448	zc40b06.r1 Soares senescent fibroblasts NbIISF Iumo
								W47282	H.sapiens fus mRNA.
44	CATGGGGGGTAACTA	H699144	3	19	15	12	5	X71428	TLS=translocated in liposarcoma [human, mRNA, 1824
								S62140	zb96a06.r1 Soares parathyroid tumor NbHPA Homo sap
								W31782	Human parathyrosin mRNA, complete cds.
								M24398	
45	CATGTCCTGCCCAT	H883029	3	19	14	27	16		Human defensin 6 (HD-6) gene, complete cds.
46	CATGAAGTGGCAAGA	H47683	0	16	0	0	0	U33317	Homo sapiens defensin 6 mRNA, complete cds.
47	CATGGGTATTACCA	H708338	0	16	0	0	0	M98331	Homo sapiens defensin 6 mRNA, complete cds.
								D32027	Human mRNA for T cell receptor V beta 14 CDR3, par
48	CATGGGCTACACCTT	H684312	2	16	0	2	1	T11701	A1225F Homo sapiens cDNA clone A1225 similar to Mi
								D51783	Human fetal brain cDNA 5'-end GEN-051G02.
49	CATGAGGGTGTTC	H175870	1	15	0	0	0	D13138	Human mRNA for dipeptidase.
50	CATGCAAGGACCAGC	H272467	0	13	0	2	0		Homo sapiens (clones MDP4, MDP7) microsomal dipept
									RDP=renal dipeptidase [human, kidney, Genomic, 357
									Human alpha-1 collagen gene, 3' end with polyA sit
51	CATGTGGAATGACC	H950498	0	13	0	167	0	M10629	ym17e04.s1 Homo sapiens cDNA clone 47962 3' simila
52	CATGATCCGCCTGCC	H219514	1	13	3	4	1	H11641	yq51a09.s1 Homo sapiens cDNA clone 199288 3' simil
								R95667	
53	CATGTCCCGTACAC	H875282	1	13	0	0	1		Human TB2 gene mRNA, 3' end.
54	CATGATGTAAAAAT	H241665	0	11	0	12	14	M74090	

										J03801	Human lysozyme mRNA, complete cds with an Alu repe
										M19045	Human lysozyme mRNA, complete cds.
55	CATGCCAGCCCGTC	H337244	0	11	0	0	0	0			
56	CATGACCAATCTGCT	H85882	0	10	1	26	3			X57351	Human I-8D gene from interferon-inducible gene fam
										X02490	Human interferon-inducible mRNA (cDNA 1-8).
57	CATGAGGACCATCGC	H165175	0	10	0	0	0	0			
58	CATGATGTGAAGAGT(A)	H243747	0	10	0	165	0			J03040	Human SPARC/osteonectin mRNA, complete cds.
59	CATGCAGTTGGTTGT	H310975	0	10	6	7	4			U55217	Human RNA fragment from patients with Crohn's dise
60	CATGGCCCTCTGCCA	H613862	0	10	2	15	7				
61	CATGTTAGATAAGCA	H992010	0	10	3	3	6			M94083	Human chaperonin-like protein (HTR3) mRNA, complet
										L27706	Human chaperonin protein (Top20) gene complete cds

Transcripts increased in both colon primary tumors and colon cancer cell lines compared to normal colon (47 genes)

NC: Normal Colon
 TU: Colon Primary Tumor
 CL: Colon Cancer Cell Line
 PT: Pancreatic Primary Tumor
 PC: Pancreatic Cancer Cell Line

#	Tag Sequence	Tag_Number	NC	CT	CL	PT	PC	Accession	Gene Name
1	CATGGCAGCCATCCG	H599350	87	180	230	72	138	U14969	Human ribosomal protein L28 mRNA, complete cds.
2	CATGATGGCTGGTAT	H239533	52	153	318	80	294	X17206	Human mRNA for L1.Rep3.
3	CATGCCCGTCCGGAA	H355689	87	142	246	178	250	X64707	H.sapiens BBC1 mRNA
4	CATGAGGCTACGGAA	H171113	44	117	167	86	147	X56932	H.sapiens mRNA for 23 kD highly basic protein
5	CATGAGCAGCTCCAG	H148949	42	116	197	103	190	Z11692	H.sapiens mRNA for elongation factor 2.
6	CATGCTGGGTTAATA	H502724	29	115	160	75	134	M81757	H.sapiens S19 ribosomal protein mRNA, complete cds
7	CATGGGATTGGCCT	H671654	55	108	222	73	185	M17887	Human acidic ribosomal phosphoprotein P2 mRNA, com
8	CATGTACCATCAATA	H807748	46	107	98	64	189	X53778	H.sapiens hng mRNA for uracil DNA glycosylase.
9	CATGTGGGCAAGCC	H959498	51	103	156	45	152	J02642	Human glyceraldehyde 3-phosphate dehydrogenase mRNA
10	CATGAATCCTGTGGA	H55227	30	95	102	48	156	Z11531	H.sapiens mRNA for elongation factor-1-gamma.
11	CATGGGACCACTGAA	H660601	36	92	114	43	63	M55409	Human pancreatic tumor-related protein mRNA, 3' en
12	CATGAGGGCTTCCAA	H174037	47	91	167	91	155	Z28407	H.sapiens mRNA for ribosomal protein L8.
								X73460	H.sapiens mRNA for ribosomal protein L3.
								M73791	Human novel gene mRNA, complete cds.
								M64241	Human Wilms tumor-related protein (QM) mRNA, comp
								S35960	Human laminin receptor homolog (3' region) [human, mRNA
								X80822	H.sapiens mRNA for ORF.
13	CATGAAGGTGGAGGA	H44683	48	91	182	113	215	X03342	Human mRNA for ribosomal protein L32
14	CATGTGCACGTTTC	H935680	45	87	105	61	122	M58458	Human ribosomal protein S4 (RPS4X) isoform mRNA, c
15	CATGTCAGATCTTG	H861056	37	81	93	50	92	M22146	Human scar protein mRNA, complete cds.
16	CATGTGGTGTGAGG	H965603	42	79	83	55	250	X69150	H.sapiens mRNA for ribosomal protein S18.
								L06432	Homo sapiens 18S ribosomal protein (HKE3) mRNA seq
								Y00052	Human mRNA for T-cell cyclophilin.
17	CATGCCTAGCTGGAT	H379369	28	77	80	46	143	X07868	Human DNA for insulin-like growth factor II (IGF-2);
18	CATGCTTGGGTTTG	518912	0	73	42	0	0	U16811	Human Bak mRNA, complete cds.
19	CATGCTCCTCACCTG	H482584	12	72	41	34	50		

20	CATGCTGTTGGTGAT	H507577	17	65	116	48	103	D14530	Human homolog of yeast ribosomal protein S28, comp
21	CATGCGCCGGAACAC	H416261	28	62	183	55	94	X73974	H.sapiens HRPL4 mRNA.
22	CATGCAATAAATGTT	H274492	9	60	73	55	119	D23661	Human mRNA for ribosomal protein L37, complete cds
23	CATGACATCATCGAT	H79065	15	57	82	42	118	L06505	Human ribosomal protein L12 mRNA, complete cds.
24	CATGTTCAATAAAAA	H1000193	12	56	154	49	99	M17886	Human acidic ribosomal phosphoprotein P1 mRNA, com
25	CATGGAACACATCCA	H528694	24	56	71	24	146	X63527	H.sapiens mRNA for ribosomal protein L19.
26	CATGTTATGGGATCT	H998030	7	55	78	35	77	M24194	H.sapiens mRNA for ribosomal protein L19.
27	CATGGCATAAATAGT	H253260	18	53	50	19	61	U14967	Human MHC protein homologous to chicken B complex
28	CATGATTCACAGTA		23	50	103	49	120	X55934	Human ribosomal protein L21 mRNA, complete cds.
29	CATGACTCCAAAAA	H119809	15	49	64	21	64	X52839	Human ribosomal protein L21 mRNA, complete cds.
30	CATGCTGTTGATTGC	H507455	9	44	54	22	40	X04347	Human mRNA for ribosomal protein L17.
31	CATGTACAAAATCGA	802871	0	42	20	0	0	X00910	Human mRNA for ribosomal protein L17.
32	CATGGAATAATGGTT	H524524	14	41	81	15	57	X61156	Human liver mRNA for IGF-II precursor (insulin-like grow
33	CATGAAGAAGATAGA	H33331	9	39	69	30	56	U02032	H.sapiens mRNA for laminin-binding protein.
34	CATGCCTTCGAGATC	H390692	12	36	51	25	86	U14970	Human colin carcinoma laminin-binding protein mRNA
35	CATGACTGGGTCTAT	H125661	5	29	25	25	38	X58965	Human ribosomal protein L23a mRNA, partial cds.
36	CATGCAGCTCACTGA	H302367	9	29	40	27	31	L10376	Human ribosomal protein S5 mRNA, complete cds.
37	CATGGTGTGTTTGTG	H769020	0	24	15	22	8	S80520	H.sapiens RNA for nm23-H2 gene.
38	CATGGTGCCTGAGC	H760291	0	22	17	44	18	X58336	Human putative NDP kinase (nm23-H2S) mRNA, complet
39	CATGGTTACATTAG	H774461	3	22	25	141	10	X00497	Homo sapiens c-myc transcription factor (pu) mRNA
40	CATGTGAAATAAAC	H918273	2	18	37	8	22	X16934	Human (clone CTG-B33) mRNA sequence.
41	CATGAAAAGAAACTT	H2056	1	16	27	11	25	Y00345	Human transforming growth factor-beta induced gene
42	CATGTGCTCCTGTT	H948604	1	15	16	11	3	X81005	Human mRNA for HLA class I locus C heavy chain.
43	CATGCTGATGGCAGA	H495251	0	14	15	8	6	W46476	Human hB23 gene for B23 nucleophosmin.
								X72718	Human mRNA for polyA binding protein.
									Human mRNA for BST-2, complete cds.
									Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone
									324128 3'.
									H.sapiens DNA for orphan TCR V-beta segment (allele

44	CATGACTCGCTCTGT	H121311	0	12	16	5	7	H121311	Soares fetal heart NbHH19W Homo sapiens cDNA clone 342926
									3'
									EST176663 Colon carcinoma (Caco-2) cell line II Homo sapiens
									cDNA 5' end
45	CATGGCCCCAAGGACC	H610466	0	12	19	82	17	AA305589	Human mRNA for actin-binding protein (filamin) (AB
46	CATGATCTTGTTACT	H229106	0	11	28	67	0	X53416	Human mRNA for fibronectin (FN precursor).
47	CATGAAAGCTGCTGGA	H40571	0	10	17	6	6	X02761	Human mRNA for fibronectin (FN precursor).
								Z26305	H.sapiens isoform 1 gene for L-type calcium channel

Transcripts increased in only colon cancer cell lines compared to normal colon (181 genes)

NC: Normal Colon
TU: Colon Primary Tumor
CL: Colon Cancer Cell Line
PT: Pancreatic Primary Tumor
PC: Pancreatic Cancer Cell Line

#	Tag Sequence	Tag Number	NC	TU	CL	PT	PC	Accession	Gene Name
1	CATGTGTGTTGAGAG	H978825	71	79	487	136	412	X16869	Human mRNA for elongation factor 1-alpha
2	CATGGCCGAGGAAGG	H615043	72	66	265	105	125	X53505	Human ribosomal protein S12.
3	CATGCAAAACCATCCA	H263478	137	83	245	36	502	X12883	Human cyokeratin 18.
4	CATGCACAAACGGTA	H278636	63	53	201	74	179	L19739	Homo sapiens metalloproteinase (MPS1)
5	CATGAAAAAATAAAA	H1	31	48	186	66	102	X83412	H.sapiens B1 mRNA for mucin.
								Z32564	H.sapiens FRGAMMA mRNA (819bp) for folate receptor
								X76180	H.sapiens mRNA for lung amiloride sensitive Na+ ch
								U08470	Human FR-gamma' mRNA, complete cds.
								U08471	Human folate receptor 3 mRNA, complete cds.
								S64030	Human L41 ribosomal protein
6	CATGTGGTCTCTG	H1027448	115	128	179	104	358	T91925	ye02102.1 Homo sapiens cDNA clone 116571 5'
7	CATGTCTCCATACCC	H906438	0	0	176	48	0	X66699	H.sapiens ribosomal protein L37a.
8	CATGAAGACAGTGGC	H33979	59	61	172	55	252	M60854	Human ribosomal protein S16
9	CATGCCGTCCAAAGGG	H374027	50	39	138	60	108	M92381	Human thymosin beta 10
10	CATGGGGGAAATCGC	H696375	90	90	136	203	231	X69181	H.sapiens mRNA for ribosomal protein L31.
11	CATGAAGGAGATGGG	H41531	30	37	133	38	161	U14968	Human ribosomal protein L27a
12	CATGGAGGGAGTTTC	H567488	38	53	112	65	142	X79234	H.sapiens ribosomal protein L11.
13	CATGCGCTGGTTCCA	H424694	42	64	111	53	49	J03537	Human ribosomal protein S6
14	CATGGCCGTGTCGCG	H618199	56	39	109	28	120	U58682	Human ribosomal protein S28 mRNA, complete cds
15	CATGGACGACACGAG	H549145	32	59	105	44	70	X52839	Human mRNA for ribosomal protein L17
16	CATGTACCCACACACC	H857362	36	48	103	44	65	U12465	Human ribosomal protein L35
17	CATGCCGCCCGGCT	H416106	39	43	90	52	184	M17885	Human acidic ribosomal phosphoprotein P0
18	CATGCTCAACATCTC	H475448	27	41	89	27	145	M23725	Human M2-type pyruvate kinase mRNA, complete cds.
19	CATGTGGCCCCACCC	H955718	20	30	80	46	55	M26252	Human TCB gene encoding cytosolic thyroid hormone-
20	CATGCCCTGGGTTCT	H359102	34	49	78	92	145	M11147	Human ferritin L chain

21	CATGAGCATCTCCAG	H150997	0	0	77	0	0	H09058	y196f1.r1 Homo sapiens cDNA clone 45943 5'.
								Z44640	H. sapiens partial cDNA sequence; clone c-26b05.
								N75111	y229e01.r1 Homo sapiens cDNA clone 284472 5'.
22	CATGGCCTGTATGAG	H621369	24	32	77	33	99	M31520	Human ribosomal protein S24 mRNA.
23	CATGAGCTCTCCCTG	H161624	33	39	76	21	67	X53777	Human L23 mRNA for putative ribosomal protein.
								gb AA223340 AA223340 Homo sapiens cDNA clone 650651 3' similar to	
								gb Y00371_mal1 HEAT SHOCK COGNATE 71 KD PROTEIN (HUMAN)	
24	CATGCCAGGAGGAAT	H338081	27	12	74	23	87	AA223340	gb Y00371_mal1 HEAT SHOCK COGNATE 71 KD PROTEIN (HUMAN)
25	CATGGCAAGCCCCA	H672342	30	55	72	27	61	U12404	Human Csa-19
26	CATGAGGAAAGCTGC	H163999	31	42	70	32	146	F16378	H. sapiens EST sequence (135-18) from skeletal muscle
27	CATGAACGCGGCCAA	H26261	29	46	69	54	79	Z23063	Homo sapiens macrophage migration inhibitory factor
28	CATGCCAGAACAGAC	H335945	23	39	66	42	148	X79238	H. sapiens ribosomal protein L30.
29	CATGCCGCCATCTC	H615736	7	10	65	10	22	U55017	Human transketolase (TKT)
30	CATGGTGTAAACCAG	H769045	16	19	65	17	76	L25899	Human ribosomal protein L10
31	CATGCCCTCGGAAAT	H383489	9	13	64	23	46	Z26876	H. sapiens ribosomal protein L38.
32	CATGAGGTCCTAGCC	H177610	15	27	63	43	41	X06547	Human class PI glutathione S-transferase
33	CATGGTCCCTGGCC	H775658	31	26	63	32	96	X65923	H. sapiens fau mRNA.
34	CATGTAAGGAGCTGA	H796831	32	58	62	42	68	X77770	H. sapiens RPS26
35	CATGAACTAAAAAA	H28673	7	14	60	17	39	W52460	zc45e11.r1 Soares senescent fibroblasts NbHSF Homo
								N92893	zb71h03.s1 Homo sapiens cDNA clone 309077 3'.
36	CATGATTTGTCCAG	H260949	17	13	57	9	91	X14957	Human hmg1 mRNA for high mobility group protein I.
37	CATGATAATTCTTTG	H200576	13	27	53	30	69	U14973	Human ribosomal protein S29
38	CATGCCCCAGCCAGT	H348756	18	23	53	5	85	U14990	Human XP1PO ribosomal protein S3 (pS3)
39	CATGGGAGTGACAT	H667269	15	13	49	13	45	L11566	Homo sapiens ribosomal protein L18 (RPL18)
40	CATGTAAAAAATAAA	H786433	13	8	48	10	26	H08238	y187a01.r1 Homo sapiens cDNA clone 44932 5'.
41	CATGGTGTGCACAA	H769605	19	21	48	21	47	X79239	H. sapiens ribosomal protein S13.
42	CATGGCCAGCCAGC	H608595	6	21	47	11	15	U31657	Human unknown protein mRNA, partial cds.
								H41030	yn92a10.r1 Homo sapiens cDNA clone 175866 5'.
43	CATGGGCTCCCACTG	H685384	14	24	47	23	15	M16660	Human 90-kDa heat-shock protein
44	CATGTCAACTTCTGG	H853983	0	0	46	2	0	N57419	yw82e04.r1 Homo sapiens cDNA clone 258750 5' simil
45	CATGGATGCTGCCAA	H583573	6	12	46	27	18	X59357	Human mRNA for Epstein-Barr virus small RNAs (EBER)
								L21756	Homo sapiens acute myeloid leukemia associated protein
								D17652	Human mRNA for HBp15/L22, complete cds.
								M64716	Human ribosomal protein S25
46	CATGAATAGGTCCAA	H51925	13	31	46	47	53	M64716	Human ribosomal protein S20 (RPS20)
47	CATGGCTTTTAAGGA	H655115	8	26	45	22	63	L06498	Homo sapiens ribosomal protein S20 (RPS20)
48	CATGAATGCAGGCAG	H585533	2	12	44	6	27	M61831	Human S-adenosylhomocysteine hydrolase (AHCY)

49	CATGGCCCCAGCTGGA	H610939	8	18	43	0	22	Z21507	Human elongation factor 1 delta (EF 1delta)
50	CATGGCCCGCGTTCG	H678334	6	6	42	8	18	M13932	Human ribosomal protein S17 mRNA
51	CATGTGAGGGAATAA	H928269	14	26	42	15	42	M10036	Human triosephosphate isomerase
52	CATGTGTACCTGTAA	H968173	14	24	42	35	49	K00358	human alpha-tubulin
53	CATGGGCAAGAAGAA	H672265	8	7	41	12	87	L19527	Homo sapiens ribosomal protein L27 (RPL27)
54	CATGAATAACAAAA	H28737	6	14	40	14	15	X63237	H.sapiens Uba80 mRNA for ubiquitin.
55	CATGATACGCTCAG	H837237	0	0	38	0	9		Unknown
56	CATGTACAAGAGGAA	H803369	7	17	38	14	42	X69391	H.sapiens ribosomal protein L6.
57	CATGGTTAACGTCCC	H770486	8	17	38	12	25	H11182	ym14a02.r1 Homo sapiens cDNA clone 47866 5'
								T40302	ya31g04.r5 Homo sapiens cDNA clone 62262 5'
								T89480	ya98a05.r1 Homo sapiens cDNA clone 116240 5'
								H01362	yi99c06.r1 Homo sapiens cDNA clone 147370 5'
58	CATGGAGACTCCTGC	H538943	13	12	38	32	10	H94371	yw34e05.r1 Homo sapiens cDNA clone 256064 5'
59	CATGATCCACATCGC	H217399	3	10	37	10	14	T49412	ya75b09.r1 Homo sapiens cDNA clone 67481 5'
								T51058	yb55a12.r1 Homo sapiens cDNA clone 75070 5'
								X07270	Human heat shock protein hsp86.
60	CATGGAAGCTTTGCA	H534522	11	13	37	14	25	M91670	Human ubiquitin carrier protein (E2-EPF)
61	CATGCTGGCGAGCGC	H501287	2	9	36	3	18	X74070	H.sapiens transcription factor BTF 3.
62	CATGCTGAGACAAAG	H493633	13	8	36	8	26	V00599	Human beta-tubulin
63	CATGAACGACCTCGT	H24951	7	13	35	22	40	X84694	H.sapiens mRNA for elongations factor Tu-mitochondria
64	CATGGCATAGGCTGC	H602783	9	16	35	2	17	L38995	Homo sapiens nuclear-encoded mitochondrial elongation factor
								S75463	P43=mitochondrial elongation factor homolog (human
								H48893	ya80b12.r1 Homo sapiens cDNA clone 202079 5'
65	CATGCATCTTCACCA	H319302	12	14	35	9	16	X71973	H.sapiens GPx-4 mRNA for phospholipid hydroperoxidase
66	CATGGCCTGCTGGGC	H621035	10	5	32	18	107	M95787	Human 22kDa smooth muscle protein (SM22)
67	CATGACAGGCTACGG	H76231	0	5	31	64	0	H80294	yu59g01.s1 Homo sapiens cDNA clone 230448 3'
68	CATGGAAATGTAAGA	H528067	5	12	31	14	25	R74294	yi57f06.r1 Homo sapiens cDNA clone 143363 5'
								L36055	Human 4E-binding protein 1
69	CAT'GGAAGCCAGCCA	H533798	1	3	30	9	11	F17005	H.sapiens EST sequence (011-T1-18) from skeletal muscle
70	CATGTTACCATATCA	H988366	10	28	30	19	86	H10519	yi90g04.r1 Homo sapiens cDNA clone 45563 5'
71	CATGTTGCTCAGAAA	H1023249	1	2	29	1	2		Unknown
72	CATGTCCCGCTCGA	H874103	0	6	29	0	0	X04409	Human coupling protein G(s) alpha-subunit
73	CATGATTAACAAAGC	H246019	8	9	29	25	26	X56998	Human Uba52 adrenal mRNA for ubiquitin-52 amino acid
74	CATGCAGATCTTGT	H298495	2	7	28	8	24	F19234	H.sapiens EST sequence (005-X3-16) from skeletal m
75	CATGGTTCGTGCCAA	H777109	9	28	28	17	46	X52317	Human histone H2A.Z.
76	CATGGACGTGTGGGC	H552683	3	4	27	2	16		

77	CATGCTAAAAA	H458753	4	8	27	19	8	M33680	Human 26-kDa cell surface protein TAPA-1
78	CATGGGTTTTATT	H704500	4	1	27	6	18	L28809	Homo sapiens dbpB-like protein
79	CATGCCGATCACCGG	H363799	7	9	27	7	15	M29536	Human translational initiation factor 2 beta subunit
80	CATGGCACAAAGA	H594051	6	9	26	7	29	W07137	za92a1.l.r1 Soares fetal lung NbHL19W Homo sapiens
								D20503	Human HL60 3'directed Mbol cDNA, HUMGS01477, clone
								N91592	Soares fetal lung NbHL19W Homo sapiens cDNA clone 303055 3'
								H83884	yy84c07.s1 Homo sapiens cDNA clone 249420 3' similar to contains Alu repetitive element;
81	CATGCTCTACCCAC	H908373	7	11	26	11	13	Z22572	H.sapiens CDEI binding protein mRNA.
								L09209	Homo sapiens amyloid protein homologue mRNA, compl
								L19597	Human binding protein mRNA, partial cds.
								S60099	APPH=amyloid precursor protein homolog (human, pla
82	CATGGTTTCCCAAG	H783697	1	0	25	3	0	W07587	zb06f02.r1 Soares fetal lung NbHL19W Homo sapiens
								N28502	yx36f06.r1 Homo sapiens cDNA clone 263843 5'
								N35630	yx62a03.r1 Homo sapiens cDNA clone 266284 5'
								Z40265	H. sapiens partial cDNA sequence; clone c-1xe03.
83	CATGCCCTGTCCAGCC	H388426	2	3	25	3	13	W02723	H. sapiens fetal heart NbHL19W Homo sapiens
								N24893	zs65e03.s1 Soares fetal heart NbHL19W Homo sapiens
								N32178	yy25b09.s1 Homo sapiens cDNA clone 269921 3'
								H21873	yl34b10.s1 Homo sapiens cDNA clone 272249 3'
84	CATGTCATCATCTGA	H865503	5	15	25	5	7	H21873	yl34b10.s1 Homo sapiens cDNA clone 160123 3' simil
								H26394	yl48e12.s1 Homo sapiens cDNA clone 161518 3' simil
								H69857	yr88d02.s1 Homo sapiens cDNA clone 212355 3' simil
								H70714	yu69b11.s1 Homo sapiens cDNA clone 239037 3' simil
								X53110	Human mRNA for neurite outgrowth-promoting protein
85	CATGCCCTGCCTTGT	H358783	5	8	25	16	31	X03168	Human mRNA for S-protein.
86	CATGGCCGGGCCCTC	H617048	1	1	24	0	1	X03168	Human mRNA for S-protein.
								AA143561	zo32d09.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 588593
87	CATGTTGCTCAAAAA	H1023233	2	1	24	2	2	AA143561	3' similar to contains LTR7.t1 LTR7 repetitive element
								AA152342	zo01g11.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 566468
								AA115727	3' similar to contains LTR7.t1 LTR7 repetitive element
								AA115727	3' similar to contains LTR7.t1 LTR7 repetitive element
								R76502	yl61f09.r1 Homo sapiens cDNA clone 143753 5'.
88	CATGCAAAATCAGGA	H262987	6	2	24	5	15	T32681	EST52915 Homo sapiens cDNA 5' end similar to None.
								T34662	EST72468 Homo sapiens cDNA 5' end similar to None.
89	CATGGAAGATGTGGG	H533435	1	5	23	4	7	H04634	yy49h03.r1 Homo sapiens cDNA clone 152117 5'.

90	CATGGTGCCTCATTTCA	H761150	0	8	23	6	4	F00364	H. sapiens partial cDNA sequence; clone 76D12; ver
								H01503	y121c05.s1 Homo sapiens cDNA clone 149384 3'
								H84813	yv86c02.s1 Homo sapiens cDNA clone 249602 3' simil
								H84936	yv88f07.s1 Homo sapiens cDNA clone 249829 3' simil
								L38961	Homo sapiens putative transmembrane protein (B5)
91	CATGGCTTTACTTTG	H654464	4	5	23	9	5	J04026	Homo sapiens putative transmembrane protein (B5)
92	CATGTTTCTGAAAG	H1046401	6	13	23	10	10	D11078	Human thioredoxin (TXN) mRNA
93	CATGTTTCTGACACA	H1023250	1	4	22	0	4	X53279	Human RGH2 gene.
94	CATGGATTCTCAGC	H589267	0	0	22	0	19	M77836	Human mRNA for placental-like alkaline phosphatase
95	CATGAGGAGGAGGC	H166539	2	3	22	2	4	X07674	Human pyrroline 5-carboxylate reductase mRNA,
96	CATGGCTTAACCTGG	H651359	3	4	22	2	4	Y00433	Human glutamate dehydrogenase
97	CATGCTCTTCGAGAA	H490889	4	8	22	27	19	X67951	Human mRNA for glutathione peroxidase
98	CATGAGAACAAACC	H132098	1	7	21	9	6	U38846	H. sapiens mRNA for proliferation-associated gene
99	CATGCCCCAGGAGAA	H346761	3	3	21	2	24	D16933	Human stimulator of TAR RNA binding (SRB)
								U42376	Human HepG2 3' region cDNA, clone hmd4f11.
								U42376	Human retinoic acid induced RIG-E
100	CATGCACTTCAAGG	H294155	0	3	20	47	107	Unknown	Human
101	CATGGCGGAGAGAG	H631331	2	3	20	4	1	F17524	Unknown
102	CATGTTACCTCTTC	H989024	4	7	20	3	22	W52942	H. sapiens EST sequence (012-T2-32) from skeletal m
103	CATGACTCTGCAAG	H122449	4	7	20	3	7	R21316	Unknown
104	CATGTCAGATGCGT	H861095	1	6	19	12	7	X00566	zc03h05.r1 Soares parathyroid tumor NbHPA Homo sap
105	CATGGGCCCTTTT	H679936	1	3	19	5	3	M80244	yg48h11.r1 Homo sapiens cDNA clone 35917 5' simila
106	CATGTGGACGCGCTG	H951912	0	0	19	0	0	H27927	Human lipoprotein apoA1.
107	CATGCCCTGCTCCCTG	H386904	0	5	19	6	5	Y558c11.s1	Human E16 mRNA
108	CATGGCCACACCCCA(C)	H607318	2	6	18	18	15	X57959	y158c11.s1 Homo sapiens cDNA clone 162452 3' simil
109	CATGATTATTTTCT	H249854	2	3	18	5	20	AA299898	H. sapiens ribosomal protein L7.
110	CATGGAAACCCTGGGA	H529899	2	7	18	5	15	U09510	EST12509 Uterus tumor 1 Homo sapiens cDNA 5' end
111	CATGGGCTGATGTGG	H686319	3	5	18	8	17	X76013	Human glycyl-tRNA synthetase.
112	CATGTCAATAAAGAA	H855049	3	10	18	4	4	W16529	H. sapiens QRSHs mRNA for glutamyl-tRNA synthetas
113	CATGAAAGTGAAGAT	H11785	0	7	17	0	5	W35192	zb10a11.r1 Soares fetal lung NbHL19W Homo sapiens
								W52451	zc70b05.r1 Soares fetal heart NbHH19W Homo sapiens
								D38251	zc45d09.r1 Soares senescent fibroblasts NbHSF Homo
								D52570	Human mRNA for RPB5 (XAP4)
114	CATGCACGCGCTCAA	H288373	0	1	17	0	3	D52758	Human fetal brain cDNA 5'-end GEN-081G12.
115	CATGAATAACTACTA	H28872	1	6	17	13	31	D55953	Human fetal brain cDNA 5'-end GEN-087A08.
								M22490	Human fetal brain cDNA 5'-end GEN-407H12.
116	CATGCTGTACTCTGGA	H504187	1	0	17	12	6		Human bone morphogenetic protein-2B (BMP-2B)

117	CATGCGACCCACGC	H398663	2	6	17	48	0	M12529	Human apolipoprotein E
118	CATGTAGAAAAATAA	H819213	0	1	16	2	7	X16539	H.sapiens RNA for neuroleukin gene.
								M27691	Human transactivator protein (CREB) mRNA, complete
								M86667	H.sapiens NAP (nucleosome assembly protein)
119	CATGATCTTGAAAGG	H228867	0	0	16	5	3	M86667	H.sapiens NAP (nucleosome assembly protein)
120	CATGCAGCTGGCCAT	H302741	0	1	16	14	0	X53743	H.sapiens mRNA for fibulin-1 C.
121	CATGATCTTGAAAGG	H228867	0	0	16	5	3	Z26328	H.sapiens partial cDNA sequence; clone HEC059
121	CATGATCTTGAAAGG	H228867	0	0	16	5	3	Z26328	H.sapiens partial cDNA sequence; clone HEC059
121	CATGATCTTGAAAGG	H762554	2	10	16	3	5	U22055	Human 100 kDa coactivator mRNA
122	CATGGTGGAGGTGCG	H762197	1	5	15	7	10	R91724	yp98e02.r1 Homo sapiens cDNA clone 195482 5' simil
123	CATGGTGGACCCCAA							W51770	zc48a02.r1 Soares senescent fibroblasts NBHSF Homo
								N42086	yy05b03.r1 Homo sapiens cDNA clone 270317 5'
								R80990	yi94c02.r1 Homo sapiens cDNA clone 146882 5'
124	CATGGAGCAGCTGGA	H561787	0	5	15	2	4	R93056	yy44f01.r1 Homo sapiens cDNA clone 198649 5' simil
								F16507	H.sapiens EST sequence (147-09) from skeletal musc
125	CATGGCGGGAGGGCT	H633002	1	6	15	8	7	T50201	yb77h05.r1 Homo sapiens cDNA clone 77241 5' simila
								S85655	Human prohibitin
126	CATGATTGGCTTAAA	H256497	1	8	15	0	16	M38188	Human unknown protein from clone pHGR74 mRNA, comp
127	CATGGAATAATTTAA	H524541	0	3	15	4	0	Y00711	Human lactate dehydrogenase B (LDH-B).
128	CATGGATCACAGTTT	H577840	0	5	15	0	0	D83174	Human collagen binding protein 2.
129	CATGAGCCTTTGTTG	H155632	1	2	15	23	5	X70940	H.sapiens elongation factor 1 alpha-2.
130	CATGTCTGCACCTCC	H910430	0	0	15	0	2	T30623	EST19638 Homo sapiens cDNA 5' end similar to None.
131	CATGAACAGAAGCAA	H18469	0	2	15	3	11	C01011	HUMGS0004747, Human Gene Signature, 3'-directed cDNA sequence.
								zm62d06.s1	Stratagene fibroblast (#937212) Homo sapiens cDNA clone
								AA111865	530219 3'
								W56516	zd16c08.r1 Soares fetal heart NbHH19W Homo sapiens
								H30299	yo77d04.r1 Homo sapiens cDNA clone 183943 5' simil
132	CATGTGTTCCAGGACC	H980130	1	1	14	5	11	H50265	yo28c02.r1 Homo sapiens cDNA clone 179234 5'
								W01702	za37a06.r1 Soares fetal liver spleen 1NFELS Homo sa
133	CATGTAGATAATGGC	H822331	1	4	14	6	14	W04495	za58b10.r1 Soares fetal liver spleen 1NFELS Homo sa
								W23528	zc71g11.s1 Soares fetal heart NbHH19W Homo sapiens
								D11838	Human HepG2 3'-directed Mbol cDNA, clone hm02e09.
								X75598	H.sapiens hm23H1 gene.
134	CATGCTTAATCCTGA	H508767	0	6	14	6	12	T35470	EST85850 Homo sapiens cDNA 5' end similar to None.
135	CATGGGCAGAGGACC	H673954	0	6	14	5	11	T35470	EST85850 Homo sapiens cDNA 5' end similar to None.
136	CATGTGACTGAAGCC	H925194	0	5	14	3	0	T35536	EST86951 Homo sapiens cDNA 5' end similar to None.

137	CATGGATAGTTGTGG	H576495	0	1	14	2	1	T35545	EST87066 Homo sapiens cDNA 5' end similar to None.
								H01694	yj33g11.s1 Homo sapiens cDNA clone 150596 3'.
								N7851	zb17d08.s1 Homo sapiens cDNA clone 302319 3'.
								N78931	za92h06.s1 Homo sapiens cDNA clone 300059 3'.
138	CATGGTGGTGGACAC	H765573	1	4	13	6	13	H90469	yv01e06.r1 Homo sapiens cDNA clone 241474 5' simil
								R76765	yi63g01.r1 Homo sapiens cDNA clone 143952 5' simil
								T35045	EST79335 Homo sapiens cDNA similar to None..
139	CATGTGGGTACCTT	H961304	0	6	13	2	9	H51447	yo31a05.r1 Homo sapiens cDNA clone 179504 5'.
								W46469	zc32c05.r1 Soares senescent fibroblasts NbHSF Homo
								W51800	zc48e04.r1 Soares senescent fibroblasts NbHSF Homo
								R33196	yh77f08.r1 Homo sapiens cDNA clone 135783 5'.
								J04799	Human prothymosin-alpha
140	CATGTTCAATTATAAT	H1003313	1	10	13	8	10	D80012	Human KIAA0190 protein
141	CATGCTTCTGTGTAC(T)	H515821	0	5	13	8	12	U02389	Human hLON ATP-dependent protease mRNA
142	CATGACTGGCGAAGT	H125315	1	5	13	2	5	T29819	EST96617 Homo sapiens cDNA 5' end similar to ATP-d
								X14850	Human histone H2A.X.
143	CATGGAAGAGCTGA	H526495	1	3	13	1	6	J04088	Human DNA topoisomerase II (top2) mRNA
144	CATGCAACTCTATGG	H269775	0	1	13	1	2	K01891	Human beta globin retrovirus-like repetitive element
145	CATGAAATTGGTGC	H16303	0	0	13	0	0	H88396	EST28e05 Homo sapiens cDNA clone 28e05
								X74796	H.sapiens p85Mcm mRNA.
146	CATGCTGCACCTTACT	H496114	1	2	13	1	8	D28480	Human mRNA for hMCM2, complete cds.
								D55716	Human B lymphoma mRNA for P1cdc47, complete cds.
147	CATGAATATTGAGAA	H53129	0	5	13	6	11	T30327	EST14849 Homo sapiens cDNA 5' end similar to None.
								T34394	EST66942 Homo sapiens cDNA 5' end similar to None.
								T47475	yb14c03.r1 Homo sapiens cDNA clone 71140 5'.
								T50289	yb14h08.r1 Homo sapiens cDNA clone 71199 5'.
								Unknown	Unknown
148	CATGTCGCCGGCGC	H890535	0	1	13	2	1	H59914	Unknown
149	CATGGGGCAGCCG	H697495	0	2	13	2	7	U33818	Human inducible poly(A)-binding protein
150	CATGCCAAGAAAGAA	H329737	0	6	12	4	4	D16891	Human HepG2 3' region cDNA, clone hmd2c11.
151	CATGTTTTTGATAAA	H1048113	0	5	12	4	12	M29882	Human apolipoprotein A-II
152	CATGTGTGGAGAGCC	H977034	0	0	12	0	0	Z49216	H.sapiens mitoxantrone-resistance associated mRNA.
153	CATGCCACGGTTAG	H345789	0	5	12	5	4	Unknown	Unknown
154	CATGAATTCCTAA	H63325	0	1	12	1	1	Unknown	Unknown
155	CATGGACCTCCGGC	H548203	0	0	12	0	0	M93651	Human set gene
156	CATGTGAATCTGGGT	H921067	0	2	11	7	8		

157	CATGTCCTTCTCCAC	H884181	0	5	11	14	8	X15804	Human alpha-actinin.
158	CATGTAATCTGTCTAC	H843485	0	4	11	2	3	T19569	609F Homo sapiens cDNA clone 609 similar to SET protein
159	CATGACGTTCTCTTC	H114144	0	0	11	1	17	Z36249	HHEA18W H. sapiens partial cDNA sequence; clone HEA18W;
160	CATGCCCTGAGTCAG	H358581	0	0	11	0	0	AA207189	zq73e07.r1 Stratagene neuroepithelium (#937231) Homo sapiens cDNA clone 647268 5' similar to TR:E16910 E16910 ENDONUCLEASE. ;
161	CATGGAATTCCTCGA	H540023	0	3	11	3	1	JN80776	za98h04.s1 Homo sapiens cDNA clone 300631 3'
								ze90d01.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 366241 3'	
								AA025809	zs85h05.s1 Soares NbHTGBC Homo sapiens cDNA clone 704313
								AA279492	3'
162	CATGGACGCCGAAC	H550274	0	1	11	6	0		Unknown
163	CATGGCGGACTGGGG	H631275	0	0	11	1	0	AA098867	zk84f04.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 489535 3' similar to SW:A5 XENLA P28824 AS PROTEIN PRECURSOR
164	CATGGGAACACACAG	H656453	0	1	11	0	2	R48460	yj67e12.r1 Homo sapiens cDNA clone 153814 5'
								AA173819	zp01c02.r1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA clone 595106 5'
165	CATGTTGGGAGCCC	H1022502	0	2	11	2	1	L19183	HUMMAC30X Human MAC30 mRNA, 3' end.
								H61710	yz24a07.s1 Homo sapiens cDNA clone 206196 3'
								H77330	yu11f12.s1 Homo sapiens cDNA clone 233519 3'
								N69482	za18d05.s1 Homo sapiens cDNA clone 292905 3'
166	CATGGCAGACATTGA	H598335	0	7	10	4	9	H41078	yp52e11.s1 Homo sapiens cDNA clone 191060 3' simil
167	CATGCACCTGAAAA	H294401	0	1	10	5	0	H04630	yj49g03.r1 Homo sapiens cDNA clone 152116 5'
168	CATGGGTTGGCAGG	H719435	0	0	10	24	0	R77027	yf66e12.r1 Homo sapiens cDNA clone 144238 5'
169	CATGTTCTCTGGGC	H1007018	0	1	10	4	12	R32331	yh68g02.s1 Homo sapiens cDNA clone 134930 3' simil
170	CATGCTGCCAGCT	-497192	0	8	10	1	10	T86566	yd77g07.r1 Homo sapiens cDNA clone 114300 5' simil
171	CATGGTGAAAAAAA	H753665	0	2	10	3	7	S77357	transcript ch111 [human, RFI,RF48 stomach cancer c
172	CATGCTGTGCAGCA	H506149	0	6	10	6	1	M34338	Human spermidine synthase
173	CATGATGTTTGTGG	-835515	0	1	10	0	2	U03911	Human mutator gene (hMSH2)
174	CATGATGTAGTAGTG	H242380	0	5	10	9	7	D55671	Human heterogeneous nuclear ribonucleoprotein
175	CATGGACCCACTACC	H545906	0	1	10	3	1	J03569	Human lymphocyte activation antigen 4F2 large subunit
176	CATGAAATAGGTTT	H12992	0	1	10	6	3	D53402	Human fetal brain cDNA 5'-end GEN-108D03.
								T61971	yb96f02.r1 Homo sapiens cDNA clone 79035 5'.
								D61243	Human fetal brain cDNA 5'-end GEN-171G06.
								N77240	yy44d02.r1 Homo sapiens cDNA clone 245571 5'.
177	CATGCCCGGCGTGGT	H371131	0	0	10	1	2	T35761	EST90898 Homo sapiens cDNA 5' end similar to EST c

178	CATGGACTGAGCTTG	H555168	0	8	10	3	3	T31901	EST40719 Homo sapiens cDNA 5' end similar to None.
179	CATGAACGCCCAAT	H6481	0	2	10	1	3	X98264	[HSMPP4] H.sapiens mRNA for M-phase phosphoprotein, mpp4, 1523bp
180	CATGATGAGGCCGGG	H232027	0	4	10	7	1		Unknown
181	CATGGCCACATCCG(A)	H610614	0	9	10	6	2	D87433	Human mRNA for KIAA0246 gene, partial cds

Table 3 - Transcripts decreased in colon cancer
**Transcripts decreased in only colon primary tumors
 compared to normal colon (51 genes)**

NC: Normal Colon
 TU: Colon Primary Tumor
 CL: Colon Cancer Cell Line
 PT: Pancreatic Primary Tumor
 PC: Pancreatic Cancer Cell Line

#	Tag sequence	Tag Number	NC	CT	CL	PT	PC	Accession	Gene Name
1	CATGGCTTATTGT	H654591	184	110	185	203	111	X00351	Human mRNA for beta-actin.
2	CATGCTAGCCTCAG	H468434	170	61	130	80	75	X04098	Human mRNA for cytoskeletal gamma-actin.
3	CATGCAAAACCATCCA	H263478	137	83	245	36	502	X12883	Human mRNA for cytokeratin 18.
4	CATGCTTCCAGCTAA	H513181	64	23	36	53	104	D00017	Human lipocortin II mRNA.
5	CATGCCCCAGTTGCT	H348922	61	27	38	37	46	X04106	Human mRNA for calcium dependent protease (small subunit)
6	CATGGATGACCCGCC	H581974	53	4	42	6	32	Z65513	H.sapiens CpG island DNA genomic MseI fragment, cl
7	CATGCTGTACAGACA	H504098	50	22	26	6	32	W61077	z30402.r1 Soares fetal heart NBHH19W Homo sapiens
8	CATGCGGACTCACTG	H427848	47	15	26	18	4	D60944	Human fetal brain cDNA 5'-end GEN-141D02.
9	CATGCCCCCGCGGAA	H349801	47	10	21	15	8		Unknown
10	CATGCCCTGGAAGAGG	H387107	46	19	39	47	14	J02783	Human thyroid hormone binding protein (p55) mRNA.
11	CATGGCCTGGCCATC	H621140	46	19	24	16	20	N33042	yy05d05.s1 Homo sapiens cDNA clone 270345 3'
12	CATGAGCAGGAGCAG	H150053	43	12	26	24	20	W07627	zb06a05.r1 Soares fetal lung NBHL19W Homo sapiens
13	CATGAACGTGCAGGG	H28235	42	6	57	2	10	X01630	Human mRNA for argininosuccinate synthetase.
14	CATGGCCGCCCTGCA	H615802	40	12	16	17	8	D43682	Human mRNA for very-long-chain acyl-CoA dehydrogen
15	CATGTGGGAGAGGA	H960651	40	5	36	10	5	D29146	Human keratinocyte cDNA, clone 173.
16	CATGGTGGCCCTTGA	H648575	38	10	20	6	39	K00557	human alpha-tubulin mRNA, 3' end.
17	CATGTGGCCATCTGC	H955615	37	5	15	19	18	AA341633	AA341633 EST47188 Fetal kidney II Homo sapiens cDNA 5' end
18	CATGCGTTCCTGGGG	H436167	35	4	36	8	0	X77956	H.sapiens Id1 mRNA.
19	CATGTGCATCTGGTG	H937452	33	9	14	13	10	X87949	H.sapiens mRNA for BiP protein.
20	CATGGTGACCTCCIT	H755160	33	7	12	6	31	J04823	Human cytochrome c oxidase subunit VIII (COX8) mRNA
21	CATGTAGCTCTATGG	H826831	33	5	18	9	13	U16798	Human Na,K-ATPase alpha-1 subunit mRNA, complete c
22	CATGGTGCCTAGGG	H760267	29	7	26	19	27	R50350	gbJR50350JR50350 yJ59c04.s1 Homo sapiens cDNA clone 153030 3'
								R50013	yJ59c04.r1 Homo sapiens cDNA clone 153030 5'.
								C02981	Human Heart cDNA, clone 3NHC0642.

23	CATGGGGCGCTGTGG	H694767	28	6	20	6	26	T31329	EST30445 Homo sapiens cDNA 5' end similar to ubiquinol cytochrome-c reductase, 6.4 kDa.
24	CATGCCCTCCAGTAC	H382130	27	6	12	3	19		Unknown
25	CATGCCCTGTGACAGC	H388627	27	3	14	8	7	H63643	yr34d11.r1 Homo sapiens cDNA clone 207189 5' simil
26	CATGTCACAGTGCT	H856806	24	5	8	17	11	W60924	zd27c08.r1 Soares fetal heart NBHH19W Homo sapiens
27	CATGAATAAAGGCTA	H49320	23	5	7	11	13	L25081	Human GTPase (rhoC) mRNA, complete cds.
28	CATGTTGTTTGA	H1031929	23	5	13	15	25	D45887	Human mRNA for calmodulin, complete cds.
29	CATGAAGGTAGCAGA	H44179	23	4	10	16	12	N62815	yy66b11.s1 Homo sapiens cDNA clone 278493 3'.
30	CATGGTGTGGGGT	H769707	21	2	5	14	10	R68653	yi14b06.s1 Homo sapiens cDNA clone 139187 3'.
31	CATGTGCAGCGCTG	H936344	21	1	5	7	13	X90858	H.sapiens mRNA for uridine phosphorylase.
32	CATGATGGCAGGAG	H238697	20	2	4	0	3	H19458	yn54c02.s1 Homo sapiens cDNA clone 172226 3' simil
33	CATGGCCAGACACC	H608326	20	1	6	1	9	T30468	EST17149 Homo sapiens cDNA 5' end similar to None.
34	CATGCTTCTGCCCC	H515990	20	0	17	3	0	V00491	Human gene for alpha 1 globin.
35	CATGACCCACGTCAG	H86453	19	2	7	22	9	X51345	Human jun-B mRNA for JUN-B protein.
36	CATGGGCTGCCTGCC	H686458	18	3	4	5	8	R72429	yy90c08.s1 Homo sapiens cDNA clone 156038 3'.
								R48449	yi67b10.s1 Homo sapiens cDNA clone 153787 3'.
								R52128	yy72b03.s1 Homo sapiens cDNA clone 154253 3'.
								X12910	Human Na ⁺ ,K ⁺ ATPase gene exons 1 - 3 (alpha III is
									Unknown
37	CATGGAGGCGCGGTG	H567660	18	2	14	6	16		Unknown
38	CATGGATGAATCCGG	H581847	17	1	3	2	2		H.sapiens HCG 1 mRNA.
39	CATGAGCCCGACAC	H153109	16	2	11	7	5	X81006	Homo sapiens porin (por) mRNA, complete cds and tr
40	CATGGTTCAGCTGTC	H774780	16	2	12	3	12	L08666	Human 78 kDa gastrin-binding protein mRNA, complet
41	CATGCCCTCGCTCAGT	H383443	16	1	8	6	7	U04627	Human BENE mRNA, partial cds.
42	CATGCAATAAAAGT	H265219	15	1	8	9	0	U17077	Human semaphorin V mRNA, complete cds.
43	CATGTGCCCGCCGCA	H940378	15	1	8	0	3	U28369	Human HepG2 3'-directed Mbol cDNA, clone s150.
44	CATGGCAGTGGCCTC	H601752	15	0	6	4	3	D12038	Human TNF-alpha inducible responsive element mRNA,
45	CATGCTGGGCTGAA	H502137	14	0	3	3	18	U77396	H.sapiens EDDR1 gene for receptor tyrosine kinase.
46	CATGGCCCATTTGGAG	H611305	13	1	6	13	17	Z29093	ye38a04.s1 Homo sapiens cDNA clone 119982 3'.
47	CATGAAGAAAACCTC	H32792	12	0	2	2	0	T94990	za25g05.s1 Homo sapiens cDNA clone 293624 3'.
								N69310	zb86c03.s1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA
									clone 310492 3'
								N98502	H.sapiens EST sequence (007-X1-01) from skeletal m
48	CATGGAATGATTCT	H538878	12	0	6	6	14	F18838	zr21b10.s1 Stratagene NT2 neuronal precursor 937230 Homo sapiens
49	CATGGCCTGGTCTT	H621272	12	0	3	3	8	AA226928	cDNA clone 664027 3'
50	CCATGGCCACACAG	H610579	11	0	1	1	0	M60047	Human heparin binding protein (HBp17) mRNA

51	CATGGGATTCCAGTT	H671052	11	0	4	3	2	W52456	zc45e09.r1	Soares senescent fibroblasts NbHSF Homo
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Transcripts decreased in both colon primary tumors and colon cancer cell lines compared to normal colon (130 genes)

NC: Normal Colon
 TU: Colon Primary Tumor
 CL: Colon Cancer Cell Line
 PT: Pancreatic Primary Tumor
 PC: Pancreatic Cancer Cell Line

#	Tag Sequence	Tag Number	NC	TU	CL	PT	PC	Accession	Gene Name
1	CATGCTCCAGCTAC	H382109	803	191	304	136	663	X12882	Human mRNA for cytokeratin 8.
2	CATGCTAAGACTTCA	H460926	708	282	402	142	497	F15636	H.sapiens mitochondrial EST sequence (002T15)
3	CATGCCCCAGGTCAC	H610997	705	58	2	2	1		Unknown
4	CATGACCCCTGGGCA	H90022	512	348	93	43	235	F16940	H.sapiens mitochondrial EST sequence (009-T1-21) f
5	CATGACATTGGGTGA	H81583	504	92	4	0	0	M10050	Human liver fatty acid binding protein (FABP) mRNA
6	CATGGCGAAACCCCTG	H622680	486	108	27	30	13	SG1953	c-erbB3= receptor tyrosine kinase {alternatively sp
7	CATGAGCCCTACAAA	H153361	367	242	132	71	204	F15506	H.sapiens mitochondrial EST sequence (1-i-02) from
8	CATGGACCCCAAGATA	H545828	276	131	0	7	0	T39321	ya04c01.r2 Homo sapiens cDNA clone 60480 5'
								H24673	y141a01.s1 Homo sapiens cDNA clone 160776 3'
									HUMGS02706 Human colon 3'directed Mbol cDNA, HUMGS02706, clone cm1673.
								D25586	ye09b02.s1 Homo sapiens cDNA clone 117195 3'
9	CATGGCCGGGTGGGC	H617195	256	88	148	144	178	X64364	H.sapiens mRNA for M6 antigen.
10	CATGTTGGGGTTTCC	H1026814	202	75	84	235	369	M11146	Human ferritin H chain mRNA, complete cds.
11	CATGCTCCACCCGAA (or G)	H479577	201	120	0	11	3	L15203	Human secretory protein (P1.B) mRNA, complete cds.
12	CATGGCAGGGCCTCA	H600670	196	68	6	32	19	X93036	H.sapiens mRNA for MAT8 protein.
									yv07h09.r1 Homo sapiens cDNA clone 242081 5' similar to SP-A39484
13	CATGATCGTGGCGGG	H224923	194	24	97	40	39	H93844	A39484 ANDROGEN-WITHDRAWAL APOPTOSIS PROTEIN RVPI,
14	CATGCAAGCATCCCC	H271574	190	99	101	30	139	F17001	H.sapiens mitochondrial EST sequence (011-T1-13) f
15	CATGGACATCAAGTC	H544012	189	33	76	57	219	Y00503	Human mRNA for keratin 19.
									zb05a11.r1 Soares fetal lung NbHL19W Homo sapiens cDNA clone
									301148 5' similar to gb:V00567 BETA-2-MICROGLOBULIN
									PRECURSOR (HUMAN);
16	CATGGTTGTGGTTAA	H782013	178	110	14	340	139	W16632	zo31h04.s1 Stratagene colon (#937204) Homo sapiens cDNA clone
								AA143804	S88535 3'

[illegible]

										AA303091	EST12940 Uterus tumor 1 Homo sapiens cDNA 3' end za52d02.r1 Soares fetal liver spleen INFLS Homo sapiens cDNA clone 296163 5'.
63	CATGGCAGCTCCTGT	H599903	43	8	17	24	13			W02429	Yz44c11.s1 Homo sapiens cDNA clone 264596 3'.
										N20325	Yz13c12.s1 Homo sapiens cDNA clone 282934 3'.
										N45127	Zb38c11.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 305876 3'.
										N90407	
64	CATGTGTCCTGGTTC	H972720	43	12	14	25	5			U03106	Human wild-type p53 activated fragment-1 (WAF1) mR zc11f01.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 322009 3'.
65	CATGACAAACCCCA	H65878	42	16	7	12	11			W37827	Gb1W153321W15332 zc16d10.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 322483 3'.
										W15332	zc04g10.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 321378 3'.
										W32410	Yw82c01.s1 Homo sapiens cDNA clone 258720 3'.
										N32312	Human sodium/potassium-transporting ATPase beta-3 Unknown
66	CATGTAGGATGGGG	H828331	41	6	11	6	9			U51478	Zp44f11.s1 Stratagene muscle 937209 Homo sapiens cDNA clone 612333 3' similar to contains Alu repetitive element;
67	CATGACTGTGGCGC	H126619	41	7	1	4	35				Yh87e04.s1 Homo sapiens cDNA clone 136734 3' similar to contains Alu repetitive element;
68	CATGGTAGCAGGTGT	H730287	40	7	13	17	24			AA180815	Yh87e04.s1 Homo sapiens cDNA clone 136734 3' similar to contains Alu repetitive element;
										R34696	Yh87e04.s1 Homo sapiens cDNA clone 136734 3' similar to contains Alu repetitive element;
										R34696	Zq06e03.s1 Stratagene muscle 937209 Homo sapiens cDNA clone 628924 3' similar to contains Alu repetitive element
										AA194497	Hbc760 Homo sapiens cDNA clone hbc760 3' end similar to nonspecific crossreacting antigen.
69	CATGAATCACAAATA	H53508	40	12	0	3	0			T11144	Zl67e01.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 509688 3' similar to TR:G189087
										AA058357	similar to none
										C05803	Zo31e02.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 588506 3'.
										AA143765	Zp45b09.s1 Stratagene HeLa cell s3 937216 Homo sapiens cDNA clone 612377 3'.
70	CATGAGGATGGTCCC	H167606	40	11	4	4	5			AA179299	

[illegible]

99	CATGTACCTCTGATT	H810468	27	5	7	11	12	X65614	H.sapiens mRNA for calcium-binding protein S100P.
100	CATGATGATGGCACC	H233106	26	0	2	0	2		emb Z6988 HSSERCA3M H.sapiens mRNA for adenosine triphosphatase, calcium
101	CATGTTCTGTAGCCC	H1014566	25	5	0	4	0	T9568	ye65c02.r1 Homo sapiens cDNA clone 122594 5'
102	CATGCCTGTCTGCCA	H388582	24	1	2	1	3	T87539	yd89f09.s1 Homo sapiens cDNA clone 115433 3'
									gb AA347726 AA347726 EST54132 Fetal heart II Homo sapiens cDNA 5' end similar to transmembrane secretory component
103	CATGTATGATGAGCA	H844682	23	4	0	1	0		
104	CATGCTGGCAAAGGT	H500747	23	0	0	0	0		Homo sapiens bone-derived growth factor (BPGF-1) m
105	CATGCTTGATTCCCA	H517078	23	4	4	17	7	L42379	H.sapiens CL 100 mRNA for protein tyrosine phosphatase
106	CATGCTTGACATACC	H516402	22	0	0	7	2	X68277	Human N-benzoyl-L-tyrosyl-p-amino-benzoic acid hydrolase
107	CATGCTGGCACATT	H649492	22	5	0	0	0	M82962	alpha subunit (PPH alpha) mRNA, complete cds
108	CATGCTCTGAATTATG	H909556	21	1	1	1	1	X16354	Human mRNA for transmembrane carcinoembryonic antigen (CEA)
109	CATGGGAAGAGCACT	H657554	21	1	1	3	3	X74570	H.sapiens mRNA for Gal-beta(1-3/1-4)GlcNAc alpha-2,3-sialyltransferase
110	CATGGCTCTTCCCCA	H646998	20	2	0	1	0	R87768	yo45d01.s1 Homo sapiens cDNA clone 180865 3' similar to contains PTRS repetitive element
								R85880	yo36g07.s1 Homo sapiens cDNA clone 180060 3' similar to contains PTRS repetitive element
111	CATGAAATCTGGCAC	H14245	20	2	0	4	3	L20826	Human I-plastin mRNA, complete cds.
112	CATGTAATTGCAAT	H802708	19	2	0	1	7	Z50751	HSB4BMR H.sapiens mRNA for B4B
								U77085	Human epithelial membrane protein (CL-20) mRNA, complete cds
								Y07909	HSPAPR H.sapiens mRNA for Progression Associated Protein
113	CATGGTGGGGGCC	H764570	18	1	1	8	2	R48529	yj64g10.r1 Homo sapiens cDNA clone 153570 5'
									EST10a24 Clontech adult human fat cell library HL108A Homo sapiens cDNA clone 10a24.
114	CATGTTATGGTGTGA	H998127	17	0	0	1	0	T27534	sapiens cDNA clone 114895 3'
115	CATGGGAGAAACAGC	H663571	17	1	2	4	0	T86124	yd84b04.s1 Homo sapiens cDNA clone 114895 3'
								zo15g05.s1	Stratagene colon (#937204) Homo sapiens cDNA clone 587000 3'
								AA131008	
								R49945	yj58g11.s1 Homo sapiens cDNA clone 152996 3'
								T57044	ya84h01.s1 Homo sapiens cDNA clone 68401 3'
116	CATGCCAACACACAGC	H328787	17	1	0	0	0		
117	CATGAGGTGACTGGG	H178299	17	0	0	0	0		
118	CATGGCCATCCTCCA	H609654	16	0	0	0	0		gb R73013 R73013 yj94a09.r1 Homo sapiens cDNA clone 156376 5'

		H1039799	I5	1	0	4	4	M69013	Human guanine nucleotide-binding regulatory protein
119	CATGTTTCTCGTCG	H860776	I5	1	1	1	0		Unknown
120	CATGTCAGAGCGCTG								yy72h06.s1 Soares fetal liver spleen 1NFLS Homo sapiens cDNA clone 248315 3' similar to contains element PTR7 repetitive element
121	CATGTTCCGCGTTCC	H1006014	I4	1	0	0	2	N58523	Unknown
122	CATGTACGGTGTGGG	H814011	I4	1	0	0	0		Unknown
123	CATGCTCAGAACTTG	H477216	I4	0	1	4	13		Unknown
124	CATGGGACTAAATGA	H662543	I3	1	0	1	0	M29540	Human carcinoembryonic antigen mRNA (CEA), complete cds.
125	CATGGCTTGGGGATT	H653988	I2	0	0	0	1	D25786	HUMGS04154 Human colon 3'directed Mbol cDNA, HUMGS04154, clone cm02115.
126	CATGACCCCAACTGCC	H861138	I2	0	0	0	1	T73613	yc36e02.r1 Homo sapiens cDNA clone 82778 5' similar to gb:L07765 LIVER CARBOXYLESTERASE PRECURSOR
127	CATGCTGAACCTCCC	H491894	I2	0	0	2	2		Unknown
128	CATGCAAGAGTTTCT	H271102	I1	0	0	2	0	AA226797	gb T95615 T95615.ye40e03.s1 Homo sapiens cDNA clone 120220 3'. zrl9b1.l.s1 Stratagene NT2 neuronal precursor 937230 Homo sapiens cDNA clone 663837 3'
129	CATGGTCCGAGTGCA	H743610	I1	0	0	8	5	AA218730	zq97h01.s1 Stratagene NT2 neuronal precursor 937230 Homo sapiens cDNA clone 649969 3'
130	CATGTTTGTTTCAC	H1043445	I1	0	0	0	0	H38178	yp57f10.r1 Homo sapiens cDNA clone 191563 5' similar to gb:M90657 TUMOR-ASSOCIATED ANTIGEN L6 (HUMAN);.

Transcripts decreased in only colon cancer cell lines compared to normal colon (78 genes)

NC: Normal Colon

TU: Colon Primary Tumor

CL: Colon Cancer Cell Line

PT: Pancreatic Primary Tumor

PC: Pancreatic Cancer Cell Line

#	Tag sequence	Tag Number	NC	TU	CL	PT	PC	Accession	Gene Name
1	CATGCACCTAATTGG	H285759	612	755	411	161	333	F15516	H.sapiens mitochondrial EST sequence (1-t-12)
2	CATGATTGAGAAGC	H260227	603	566	158	249	173	F12396	H. sapiens partial cDNA sequence; clone c-39e04.
3	CATGTGATTTCACCT	H933704	452	595	235	80	314	L08441	Human autonomously replicating sequence (ARS) mRNA
4	CATGTTCATACACCT	H1002566	444	357	114	64	191	F15553	H.sapiens mitochondrial EST sequence (001T14)
5	CATGCCACTGCACCT	H335432	385	402	223	278	132	X51525	Human cortex mRNA containing an Alu repetitive element
6	CATGACTAACACCCCT	H114966	369	446	171	76	161	F16402	H.sapiens mitochondrial EST sequence (141-20)
7	CATGCACTACTCACC	H291282	293	527	78	14	83	U09500	Human mitochondrial cytochrome b gene, partial cds
8	CATGAAAACATTCTC	H478249	200	169	98	17	223	F15744	H.sapiens mitochondrial EST sequence (101-03)
9	CATGCTCATAAGGAA	H885334	147	183	94	21	75	F15511	H.sapiens mitochondrial EST sequence (1-t-07)
10	CATGTCGAAGCCCCC	H103075	145	160	91	49	57	F18587	H.sapiens mitochondrial EST sequence (022T19)
11	CATGACGCGAGGAGA	H1025322	124	194	63	69	47	H03983	yj47a08.s1 Homo sapiens cDNA clone 151862 3'.
12	CATGTTGGCCAGGCT	H1027595	98	106	17	183	107	M17733	H.sapiens mRNA for MHC class II transactivator.
13	CATGTTGGTGAAGGA	H214616	97	186	17	41	49	U46913	Human EST overexpressed in pancreatic cancer (xs31)
14	CATGATCAGCCCTC	H941638	67	48	25	75	34	X05607	Human mRNA for cysteine proteinase inhibitor precursor
15	CATGTGCCTGCACCA	H136465	64	121	28	24	15	D54113	Human fetal brain cDNA 5'-end GEN-129B05.
16	CATGAGACCCACAAC	H196339	60	33	17	13	15	X14758	Human mRNA for adenocarcinoma-associated antigen
17	CATGAGTTTGTAGT	H656389	56	41	4	31	3	L33930	Homo sapiens CD24 signal transducer mRNA
18	CATGGGAACAACAG	H965434	53	271	6	30	5	D50954	Human fetal brain cDNA 3'-end GEN-002A10.
19	CATGGGTGTATGCA	H527436	49	35	10	100	36	M11233	Human cathepsin D mRNA, complete cds.
20	CATGGAAATACAGTT	H763719	49	37	21	27	15	U25801	Human Tax 1 binding protein mRNA, partial cds.
21	CATGGTGCTCACGC	H765509	45	26	18	23	15	U31215	Human metabotropic glutamate receptor 1 alpha
22	CATGGTGGTGACAC	H704160	44	56	2	6	1	S79597	hRNAser(UNC) [human, muscle, MERRF/MELAS overlap s
23	CATGGGGTTGGCTTG	H763567	42	32	15	20	5	T48809	y005603.r1 Homo sapiens cDNA clone 70276 5' contai
24	CATGGTGGCGGGTGC	H821029	39	23	1	23	10	M69023	Human globin gene.
25	CATGTAGACTAGCAA								

26	CATGGCTAGGTTTAT	H641789	38	144	13	25	13	D51017	Human fetal brain cDNA 3'-end GEN-007C04.
27	CATGGGCTTTAGGGA	H687915	37	372	6	29	11	W15552	zb91h11.s1 Soares parathyroid tumor NbHPA Homo sap
28	CATGGGGGTCAAGG	H699691	37	170	11	16	9	F16326	H.sapiens mitochondrial EST sequence (132-20) from skeletal muscle
29	CATGATTTTCTAAAA	H261569	33	13	11	8	2	AA315049	EST186995 HCC cell line (metastasis to liver in mouse) II Homo sapiens cDNA 5' end
30	CATGGACTTGCCCT	H294488	33	18	11	17	36	F01150	H. sapiens partial cDNA sequence; clone A6A03; ver
31	CATGCCCTGTCAGG	H386963	32	13	0	6	2	N29971	yw53h01.s1 Homo sapiens cDNA clone 255985 3'.
32	CATGAGAACCTTCCA	H132598	32	14	3	16	12	K02883	Human MHC class I HLA-A2 gene, complete cds.
33	CATGCTCTGCCCTC	H489822	32	32	7	20	5	R09140	yf23f12.s1 Homo sapiens cDNA clone 127919 3'.
								R76005	yf22c10.s1 Homo sapiens cDNA clone 158994 3'.
								T33596	EST58371 Homo sapiens cDNA 3' end similar to None..
34	CATGGCCATCCCTT	H609624	29	73	7	14	16	F16449	H.sapiens mitochondrial EST sequence (129-09)
35	CATGGCCACGCGCC	H610922	28	9	1	1	7	AA292959	z154f10.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 726187 3'
36	CATGTGGCGCTGTC	H956860	26	8	1	1	2	AA292466	z31c11.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 723956 5' similar to TR:G205858 G205858 RAT ORF
									zb62a07.s1 Soares fetal lung NbHL19W Homo sapiens cDNA clone 308173 3' similar to PIR:A39484 A39484 androgen-withdrawal apoptosis protein RVP1, prostatic - rat
								N92384	zb19c06.s1 Homo sapiens cDNA clone 302506 3' similar to PIR:A39484 A39484 androgen-withdrawal apoptosis protein RVP1, prostatic - rat ;
								N80203	z139d06.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 485195 3' similar to PIR:A39484 A39484 androgen-withdrawal apoptosis protein RVP1
								AA039323	Human partial cDNA sequence with CCA repeat region
37	CATGAGGGTGTTC	H175872	26	218	7	20	10	U21468	Human epistatin variant A mRNA, 3' end.
38	CATGCCCTGGAGTG	H387596	25	10	0	45	17	M34088	Unknown
39	CATGAGTCTGCTGGA	H188027	24	9	1	0	0		
40	CATGCCCGCCTCTTC	H353760	24	11	2	3	4	T10098	seq816 Homo sapiens cDNA clone b4HB3MA-COT8-HAP-Ft
41	CATGAAAAGAGTGGT	H2235	22	9	2	0	7	X83228	H.sapiens mRNA for LI-cadherin.
42	CATGGCCACGTGGAG	H607977	21	7	1	2	2	L27415	Homo sapiens huntingtin (HD) gene, exon 66.
								C00470	dbjC00470C00470 HUMGS0007620, Human Gene Signature, 3'-directed cDNA sequence.
43	CATGAGGATGTGGG	H167659	21	5	4	1	3	N63531	y762g08.s1 Homo sapiens cDNA clone 278174 3'.

[illegible]

62	CATGGGGCTACGTC	H695406	14	4	0	1	0	M25629	Human kallikrein mRNA, complete cds, clone clone p
63	CATGCCCGGCTCCTC	H354776	14	7	1	5	2	H18336	ym45d10.s1 Homo sapiens cDNA clone 51262 3'.
								zk01e10.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 469290 3'.	
								AA026974	clone 469290 3'.
									zu12c12.r1 Soares testis NHT Homo sapiens cDNA clone 731638 5' similar to gb:M61900 Human prostaglandin D synthase gene, complete cds. (HUMAN);
								AA405031	complete cds. (HUMAN);
64	CATGAGGTACTACTA	H176584	13	9	0	9	8	U66894	gbU66894 H5U66894 Human epithelium-restricted Ets protein ESX mRNA,
								U73843	Human epithelial-specific transcription factor ESE-1b (ESE-1)
65	CATGCAAAATAAATTA	H265232	13	3	0	1	0	D25996	mRNA, complete cds
66	CATGCTGTAAAAAAA	H503809	13	6	0	1	1		Human colon 3'directed Mbol cDNA, HUMGS06772
									Unknown
67	CATGGTTCAATCCCT	H774358	13	3	0	2	0	AA071520	ze88g07.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 366108 3'.
									za90h10.s1 Soares fetal lung NbHL19W Homo sapiens cDNA clone 299875 3'.
								N90742	
								AA086292	zn52h06.s1 Stratagene muscle 937209 Homo sapiens cDNA clone 561851 3'.
68	CATGAATAAAGCCTT	H49304	12	4	0	0	0	D11499	Human HepG2 3'-directed Mbol cDNA, clone a-35.
69	CATGGGAAGGTTTAC	H658173	12	2	0	1	0	T16031	IB2474 Homo sapiens cDNA 3'end.
70	CATGGGATGGCTTAT	H670333	12	1	0	6	1	T74426	yc82e01.r1 Homo sapiens cDNA clone 22306 5'.
71	CATGGGTGGCCCGGG	H715099	12	2	0	3	2	N73771	za61h02.s1 Homo sapiens cDNA clone 297075 3'.
								zh75f08.s1 Soares fetal liver spleen INFLS S1 Homo sapiens cDNA clone 417927 3'.	
								W90388	
								F03786	H. sapiens partial cDNA sequence; clone c-29h08.
72	CATGTACTGTACTTC	H817952	12	2	0	0	0	U14631	Human 11 beta-hydroxysteroid dehydrogenase type II
73	CATGCCCTTGCACTC	H360008	11	6	0	3	3	T41121	ya31a06.s5 Homo sapiens cDNA clone 62194 3' contains Alu repetitive element.
74	CATGCGGTGGGACCA	H440966	11	4	0	2	0		Unknown
75	CATGCCCGCCCAACCA	H611590	11	2	0	0	0		Unknown
76	CATGCCCGCGCTC	H616862	11	2	0	0	0	Z58486	Unknown
77	CATGGGAGGCGCTCA	H666014	11	1	0	0	0		Unknown

78	CATGTCCTCCCGTTACA	H874226	11	11	0	0	0	0	W68073	zd42c12.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 343318 3' similar to contains Alu repetitive element;
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Table 4 - Transcripts increased in pancreas:cancer -
SAGE Tags elevated only in Pancreatic Tumor

NC: Normal Colon
 Tu: Colon Tumor
 CC: Colon Cancer Cell Line
 PT: Pancreatic Tumor
 PC: Pancreatic Cell Line

	Tag Sequence	Tag Number	NC	Tu	CC	PT	PC	Examples	Accession	Gene Name
1	CATGAAGCAACCA	H9222	0	6	1	3	11		R38305	yh9504.s1 Homo sapiens cDNA clone 137455 3'
									AA126719	zk95003.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 490541 3'
									AA044296	zk51c03.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 486340 3'
									AA131586	zl33c08.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 503726 3'
									AA157983	zo71h12.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 592391 3'
2	CATGAAGCAGTTTA	H9408	1	5	2	21	3	Examples	AA292929	z54c04.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 726174 3'
									AA159306	zo78c07.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 154129 3'
									R54012	yj70h01.s1 Homo sapiens cDNA clone 79335 3'
									T62936	yb99f08.s1 Homo sapiens cDNA clone 79335 3'
									X52426	H. sapiens mRNA for cytokeratin 13
3	CATGAAGCGGGCT	H9898	0	0	0	0	13	Examples	X51698	H.sapiens spasmodic polypeptide (SP) mRNA
4	CATGAATCCTGGT	H13803	0	1	1	16	2	Examples	N70419	za61d12.s1 Homo sapiens cDNA clone 297047 3'
5	CATGAATGGACAAC	H14865	0	0	1	0	13	Examples	AA411599	zv16g01.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 753840 5'
									AA410508	zv16g01.s1 Soares NhHMPu S1 Homo sapiens cDNA clone 753840 3'
									AA115723	zl86g12.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 511558 3'
6	CATGAACCAAGTTGT	H21247	1	1	6	8	13	Examples	AA132875	zo19e04.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 587358 3'
									AA147677	zo44a06.s1 Stratagene endothelial cell 937223 Homo sapiens cDNA clone 589714 3'

[illegible]

										AA279290	z84a06.s1 Soares NbHTGBC Homo sapiens cDNA clone 704146 3'
										AA046253	zF12a02.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 376682 3'
										Z58016	H.sapiens CpG DNA, clone 26c7.
15	CATGACCACTCAATA	H67396	2	7	16	37			Examples		zo29c02.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 588290 3' similar to SW:B13 MOUSE P28662 BRAIN PROTEIN I3
										AA151668	za07c06.r1 Soares melanocyte 2NbHM Homo sapiens cDNA clone 291874 5'
										W02958	zo70e05.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 592256 3'
16	CATGACACCTGTGC	H71151	0	1	0	2	14		Examples	AA1556464	ze90h09.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 366305 3'
										AA025673	za89h12.s1 Homo sapiens cDNA clone 299783 3'
										N70895	Human interferon-inducible mRNA (cDNA 9-27): membrane
17	CATGACCATTTGGATT	H85924	0	8	5	13	4		Examples	X02491	Human interferon-inducible protein 9-27 mRNA
										J04164	H.sapiens mRNA for interferon-induced 17kDa membra
										X84958	H.sapiens HLA-E gene.
										X56841	H.sapiens mRNA for HLA-E heavy chain (exons 4 - 7)
18	CATGACCCCTTTAACA	H90050	1	4	2	13	7		Examples	X64879	Human neutrophil cytochrome b light chain p22A
										M21186	Human p22-phox (CYBA) gene, exons 3 and 4
19	CATGACGCCCGTGGT	H91579	49	22	45	70	94		Examples	M61107	Human Pro-urokinase gene.
										D00244	Human urokinase gene, 3' end
20	CATGACCTGTGACCA	H97158	0	3	0	28	17		Examples	K02286	Human pro-urokinase mRNA, complete cds
										M15476	Human uPA gene for urokinase-plasminogen activator
										X02419	Human myotonic dystrophy kinase (DM kinase) gene
21	CATGACGCCCTGCTC	H103912	0	1	0	11	2		Examples	L08835	Homo sapiens myotonic protein kinase (DM) mRNA
										M87313	yo73f06.s1 Homo sapiens cDNA clone 183779 3'
22	CATGACGTTGGTGATG	H113380	2	4	4	5	20		Examples	H44451	zo42f07.s1 Stratagene endothelial cell 937223 Homo sapiens cDNA clone 589573 3' similar to SW:L10K_RAT Q05310 LEYDIG CELL TUMOR 10
										AA157329	KD PROTEIN
											zc32g06.s1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 324058 3' similar to SW:L10K_RAT Q05310 LEYDIG CELL TUMOR 10
										W46455	KD PROTEIN

		H119383	0	0	3	21	3	Examples	M92357	Homo sapiens B94 protein mRNA, complete cds.
23	CATGACTCAGCCCGG	H119383	0	0	3	21	3	Examples	M92357	Homo sapiens B94 protein mRNA, complete cds.
24	CATGACTGAGGAAG	H123521	0	0	0	53	22	Examples	X64875	H.sapiens mRNA for insulin-like growth factor binding protein 3
										Human growth hormone-dependent insulin-like growth factor binding protein 3
									M31159	Human insulin-like growth factor-binding protein-3
									M35878	Human insulin-like growth factor binding protein 3 (3' region)
									S56205	insulin-like growth factor binding protein 1 (ECM1) mRNA
								Examples	U65932	Human extracellular matrix protein 1 (ECM1) gene, exon 9
25	CATGACTGCCCGCTG	H124264	1	0	0	22	9	Examples	U65937	Human extracellular matrix protein 1 (ECM1) gene, exon 9
										zo03f09.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 566633
								Examples	AA148916	3'
26	CATGACTGTATTTTC	H126208	3	4	9	2	22	Examples	AA148916	3'
										zo12a11.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 586652
									AA129137	3'
										zl85g09.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 511456
									AA115437	3'
										zl87e07.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 511620
									AA126967	3'
								Examples	R24613	yh36c03.r1 Homo sapiens cDNA clone 131812
27	CATGAGCACTGCAGC	H149395	1	2	6	3	16	Examples	R24613	yh36c03.r1 Homo sapiens cDNA clone 131812
28	CATGAGCAGGACGT	H150055	1	0	0	0	15	Examples	H43243	yp05e05.s1 Homo sapiens cDNA clone 186560 5'
29	CATGAGCTGTATTCT	H162622	0	2	0	1	11	Examples	X54942	H.sapiens cks2 mRNA for Cks1 protein homologue
								Examples	AA044081	zk50g07.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 486300 3'
								Examples	AA044081	zk50g07.r1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 486300 5' similar to PIR:A40533 A40533 cAMP-dependent protein kinase major membrane substrate
									AA044211	Class A ₁ Human mRNA for thrombospondin.
								Examples	X14787	yh64f11.s1 Homo sapiens cDNA clone 134541 3'
31	CATGAGTCTTCAAT	H178129	4	2	0	60	2	Examples	R27738	yh64f11.s1 Homo sapiens cDNA clone 134541 3'
32	CATGAGGTGCGGGG	H178603	0	2	2	1	11	Examples	H00276	yj22f12.s1 Homo sapiens cDNA clone 149519 3' similar to SP:ZK637.5
										CE00436 ARSA
										zm19d07.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 526093 3'
								Examples	AA076235	526093 3'
33	CATGAGTATCTGGGA	H183787	3	3	1	15	73	Examples	H13159	yj16c04.s1 Homo sapiens cDNA clone 148902 3'
										zo71e11.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 592364 3'
									AA146632	H.sapiens SA mRNA
								Examples	X80062	Human annexin V (ANX5) gene
34	CATGATACITTAATT	H204740	1	0	3	18	9	Examples	U01691	Human annexin V (ANX5) gene

47	CATGCAGCCTGGGC	H300971	0	0	0	0	0	0	0	0	10	Examples	AA149942	zo68d04.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 592039 3' similar to TR:E218488 E218488 TRYPTASE
48	CATGCAGCGGCCCT	H301462	4	11	12	10	21					Examples	AA187553 M16937	zp66b09.r1 Stratagene endothelial cell 937223 Homo sapiens cDNA clone 625145 5' similar to gb:M16937 HOMEOBOX PROTEIN HOX-B7 (HUMAN); contains element MER22 repetitive element Homeobox protein HOX-B7
49	CATGCAGGTTGTCT	H307126	0	0	4	0	10					No Match		Human ribosomal protein S10 mRNA
50	CATGCAGTCTCTCA	H309109	2	6	6	2	17					Examples	U14972	Human leukotriene A4 hydrolase gene
51	CATGCATCCCGTGAC	H316857	0	3	3	3	13					Examples	U27293	Human leukotriene A-4 hydrolase mRNA, complete cds
													J03459	Human leukotriene A-4 hydrolase mRNA, complete cds
													J02959	H. sapiens mRNA for emerin
52	CATGCATTCCTCCTT	H325080	0	2	5	13	3					Examples	X82434	Human serum constituent protein (MSE55) mRNA
53	CATGCCACCCACC	H333138	3	7	17	18	2					Examples	M88338	Human ribosomal protein S9 mRNA
54	CATGCCAGTGGCCCG	H339606	23	11	37	22	56					Examples	U14971	Human ribosomal protein S9 mRNA
55	CATGCCATTCTGG	H344031	0	2	6	1	10					Examples	L01697	Homo sapiens alpha-1 type XV collagen mRNA
56	CATGCCCAAGCTAGC	H344691	19	8	8	18	44					Examples	X54079	Human mRNA for heat shock protein HSP27.
													Z23090	H. sapiens mRNA for 28 kDa heat shock protein
													X16477	Human mRNA fragment for estrogen-regulated 24k protein
													S74571	estrogen receptor-related protein=27-kDa heat shock protein
													X69392	H. sapiens mRNA for ribosomal protein L26.
57	CATGCCCATCCGAAA	H347489	20	15	43	19	61					Examples	L07287	H. sapiens mRNA for ribosomal protein L26 (RPL26) gene
58	CATGCCCCCTGCAGA	H350099	0	1	6	14	25					Examples	U40434	Human ribosomal protein L26 (RPL26) gene
													D49441	Human mesothelin or CAK1 antigen precursor mRNA
59	CATGCCCGCATAGAT	H353481	0	0	0	8	11					Examples	U12819	Human mRNA for pre-pro-megakaryocyte potentiating factor, complete cds.
													U38945	Human p16-INK4 (p16) gene
													S69804	Human hypothetical 18.1 kDa protein (CDKN2A) mRNA
													S69822	MTS1= multiple tumor suppressor 1/cyclin-dependent kinase 4 inhibitor p16
													S78535	CDK41=cyclin-dependent kinase 4 inhibitor tumor suppressor gene, P16/MTS1/CDKN2=cell cycle negative regulator beta form
60	CATGCCCTCCTGGGG	H357867	8	2	5	14	34					Examples	Z47319	H. sapiens mRNA for expressed sequence tag (clone 21f7119)

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								M11233	Human cathepsin D mRNA, complete cds y42f03.s1 Homo sapiens cDNA clone 110909 3' similar to SP:R151.9 CE00827
S	CATGGAATGATGAG	H527929	4	7	5	14	26	Examples T90296	
'1)	CATGGAAGTGTGG	H533436	3	7	16	6	28	Examples AA181811	EEST32523 Adipose tissue, brown Homo sapiens cDNA 3' end zp64f07.s1 Stratagene endothelial cell 937223 Homo sapiens cDNA clone 624997 3'
NV	CATGGAATTATAA	H540621	6	3	10	9	28	Examples L21950 M36035	z106c06.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 491530 3' similar to WP-ZK652.2 CE00448 Human peripheral benzodiazepine receptor related mRNA Human peripheral benzodiazepine receptor (hpbs) mRNA
NNI	CATGGACAAAAAAA	H540673	1	2	10	3	17	No Match U19718	Human microfibril-associated glycoprotein (MFAP2).
N2	CATGGACCCTTTTA	H545152	0	1	0	11	2	Examples M75165	H.sapiens epithelial tropomyosin (TM1) mRNA
N3	CATGGACCAGGCCCT	H545430	0	3	0	20	18	Examples M12125 M74817	Human fibroblast muscle-type tropomyosin mRNA Human tropomyosin-1 (TM-beta) mRNA, complete cds Human cyclin mRNA
N4	CATGGACCCCAAGGC	H546039	2	5	9	16	10	Examples L37033	Homo sapiens FK-506 binding protein homologue zb37g07.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 305810 3'
N5	CATGGACCCTGCCCT	H546710	31	36	20	71	65	Examples N90046	z106a10.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 491514 3'
N6	CATGRACCTATCTCT	H548062	0	1	0	13	1	Examples AA115048 M63193	Human platelet-derived endothelial cell growth factor Human gamma-tubulin mRNA,
N7	CATGGACGGCGCAGG	H551315	3	4	5	32	3	Examples M61764	Human mRNA (HA1753) for ORF
N8	CATGGACTCTCTGTT	H554876	1	4	3	0	14	Examples DI7793 S68252	TIMP-1=metalloproteinase inhibitor EPA glycoprotein (erythroid-potentiating activity) tissue inhibitor of metalloproteinase 2
N9	CATGGAGAGCTTTGC	H559615	0	0	0	2	10	Examples X02598 X03124	
N10	CATGGAGAGTGTCG	H560056	0	5	8	32	11		
'11)	CATGGAGCACGATGA	H561807	0	0	0	1	12	No Match	
'12	CATGGAGGGAGTCCC	H567486	1	1	0	4	13	Examples N30324 X70070 H57673	zr89d01.s1 Soares NbHTGBBC Homo sapiens cDNA clone 682848 3' yw75d01.s1 Homo sapiens cDNA clone 258049 3' H.sapiens mRNA for neurotensin receptor. yr27a10.s1 Homo sapiens cDNA clone 206490 3'
'13	CATGGAGTCCGAGC	H570787	0	0	2	1	10	Examples	
'14	CATGGAGTTATGTTG	H572656	0	0	3	0	10	Examples	

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										J00202	human bla-dr heavy chain gene; 3' flank
11	CATGGGTGGGAGAT	H715401	1	4	10	10	14		Examples	U18009	Human chromosome 17q21 mRNA clone LF113.
										T33413	EST57778 Homo sapiens cDNA 3' end similar to None
										T33339	EST57474 Homo sapiens cDNA 3' end similar to None
									Examples	M59911	Human integrin alpha-3 chain mRNA
12	CATGGTACTGTAGCA	H728778	3	3	1	16	30		Examples	X87689	H. sapiens mRNA for putative p64 CLCP protein
13	CATGGTACTGTGGCT	H728810	23	10	16	15	50		Examples	L12350	Human thrombospondin 2 (THBS2) mRNA
14	CATGGTCAAAATTC	H737344	0	0	0	10	1		Examples	D21261	Human mRNA (HA1756) for ORF
15	CATGGTCTGGGGCTT	H752296	25	35	45	76	29		Examples	D29543	Human keratinocyte cDNA, clone 686
									Examples	H51290	yp07a05 s1 Homo sapiens cDNA clone 186704 3'
16	CATGGTCTGTGAGAG	H752521	0	5	7	12	2		Examples	N20338	yx44g12 s1 Homo sapiens cDNA clone 264646 3'
										AA158271	zo76c09 s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone
									No Match		
17	CATGGTCTGTGCAGG	H752531	0	0	0	1	13		No Match		
18	CATGGTCTTGAAGCC	H753162	0	1	2	1	10		Examples	X87373	Class C, H. sapiens RPS3a gene
19	CATGGTGAAGGCAGT	H754323	25	14	42	15	89		Examples	X08058	GLUTATHIONE S-TRANSFERASE P (HUMAN)
20	CATGGTGAATGACGG	H754567	0	2	8	1	10		Examples	X51439	Human mRNA for serum amyloid A (SAA) protein
21	CATGGTGCAGGAGAC	H760361	0	3	2	11	25		Examples	U15008	Human SnRNP core protein Sm D2 mRNA
22	CATGGTGCTGGAGAA	H761481	2	9	9	13	26		Examples	U62800	Cystatin M (CST6)
23	CATGGTGGAGGCAC	H762533	1	1	3	6	34		Examples	H46430	yo12h12 s1 Homo sapiens cDNA clone 177767 3'
24	CATGGTGGTACAGGA	H765003	14	17	15	39	30		Examples	AA047563	zf13a06 s1 Soares fetal heart NbtH19W Homo sapiens cDNA clone
										AA130701	376786 3'
									Examples	X59288	zo13f02 s1 Stratagene colon (#937204) Homo sapiens cDNA clone 586779
25	CATGGTTCACATGCAG	H774629	0	2	1	13	3		Examples	M24283	H. sapiens gene for intercellular adhesion molecule
										J03132	Human major group rhinovirus receptor (HRV) mRNA
										M35100	Human intercellular adhesion molecule-1 (ICAM-1)
									Examples	K02765	Human cell surface glycoprotein P3 58 mRNA
26	CATGGTTGTCTTTGG	H781823	1	1	6	30	24		Examples	M17987	Human complement component C3 mRNA, alpha and beta
27	CATGGTTGTGGTTAA	H782013	178	110	14	340	139		Examples	D00760	Human beta-2-microglobulin gene
28	CATGGTTTAAATCGA	H782391	1	6	12	4	14		Examples	X57025	Human mRNA for proteasome subunit HC3
									Examples		INSULIN-LIKE GROWTH FACTOR IA PRECURSOR (HUMAN)
29	CATGTAAGGCTTAAC	H797169	0	0	6	1	12		No Match		
30	CATGTAATTTTGGAA	H802793	0	2	5	2	10		No Match		

	CATGTAATTTTGGAT	H802793							No Match	X85373	H.sapiens mRNA for Sm protein G
		H806901	1	4	2	3	14		Examples		
11	CATGTACATTTTCAT	H808370	0	1	4	0	10		No Match		
12	CATGTACCCCGTACA	H808925	0	0	0	17	7		No Match		
13	CATGTACCCCTTCTAT	H827437	1	0	5	5	24		Examples	J02931	Human placental tissue factor (two forms) mRNA
14	CATGTAGGAAGTAA									M16553	Human tissue factor mRNA, complete cds
										M27436	Human tissue factor gene, complete cds
										X64899	H.sapiens mRNA homologous to mouse P21 mRNA
15	CATGTAGTTGTCTA	H831416	49	61	61	89	130		Examples	X16064	Human mRNA for translationally controlled tumor protein
										L13806	Homo sapiens (clone 04) translationally controlled tumor protein
										M98479	Human transglutaminase mRNA
16	CATGTATATTTTCTC	H839672	1	0	3	8	16		Examples	D12149	Human HepG2 3'-directed Mbol cDNA, clone s247
17	CATGTATTTTCTGCC	H851834	0	1	2	16	3		Examples	X80909	H.sapiens alpha NAC mRNA
18	CATGTCACAGCATA	H856209	10	28	27	24	48		Examples	X56134	Human mRNA for vimentin.
19	CATGTCCAAATCGAT	H868569	0	1	0	43	17		Examples	Z19554	H.sapiens vimentin gene
										M14144	Human vimentin gene, complete cds
										M25246	Human vimentin (HuVim3) mRNA, 3' end
										N97906	2b57a08.s1 Homo sapiens cDNA clone 307670 3'
20	CATGTCCACTGGCCT	H870310	0	0	1	12	2		Examples		
										T17488	NIB978 Normalized infant brain, Bento Soares Homo sapiens cDNA 3' end
										AA349906	EST56900 Infant brain Homo sapiens cDNA 3' end
										X67016	H.sapiens mRNA for amphiglycan
21	CATGTCCATCTGTTG	H871920	6	6	10	25	5		Examples	D13292	Human mRNA for ryudocan core protein
										M77233	Human ribosomal protein S7 mRNA
22	CATGTGCTCTTATC	H899060	2	5	15	1	69		Examples	S48568	tissue inhibitor of metalloproteinase 2 (3'-end region)
23	CATGTCTCTGATGCT	H908858	1	5	2	46	19		Examples		
										N71680	y293b03.s1 Homo sapiens cDNA clone 290573 3'
24	CATGTCTTGTAAGT	H916232	0	4	3	1	13		Examples	X03083	Human lactate dehydrogenase-A gene
25	CATGTCTTGTCATA	H916372	14	22	15	20	45		Examples	X02152	Human mRNA for lactate dehydrogenase-A
										X02153	Human pseudogene for lactate dehydrogenase-A
26	CATGTGAAGTCACTG	H920392	1	1	6	0	16		No Match		
27	CATGTGAAGTTATAC	H920525	0	1	3	6	11		Examples	X07979	CTGTGG, Class A, Human mRNA for fibronectin receptor beta subunit.

158	CATGTGATGCTGGT	H932731	0	8	3	11	12	Examples	AA027860	469693 3'	zk05h07.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone
159	CATGTGCCATCTGTA	H938876	1	3	7	3	16	Examples	M25753	G2/MITOTIC-SPECIFIC CYCLIN B1 (HUMAN)	
									T60151	yc22c04.s1 Homo sapiens cDNA clone 81414 3'	
									R67969	yt29g08.s1 Homo sapiens cDNA clone 140702 3'	
										zo91f03.s1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA clone 594269 3' similar to SW:NGAL_HUMAN P80188 NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN PRECURSOR	
160	CATGTGCCCTCAAAA	H939841	11	13	3	13	43	Examples	AA169614	zb15408.s1 Homo sapiens cDNA clone 302127 3' similar to SW:NGAL_HUMAN P80188 NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN PRECURSOR	
		H939849	3	4	0	11	19	Examples	N79823		
161	CATGTGCCCTCAGAA									zm90h04.s1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA clone 545239 3' similar to SW:NGAL_HUMAN P80188 NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN PRECURSOR	
162	CATGTGCCCTCAGGA	H939851	13	31	10	25	83	Examples	AA075896		
162	CATGTGCCCTCAGGC	H920392						No Match		zl81e07.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 511044 3'	
163	CATGTGCCCTTACTTT	H941856	0	3	1	2	12	Examples	AA100279		
164	CATGTGCGCTGCCCC	H944038	2	5	2	17	3	No Match		zk10a01.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 470088 3'	
165	CATGTGCTTCATCTG	H949560	2	6	6	4	16	Examples	AA029262	yv6e10.s1 Soares fetal liver spleen INFLS Homo sapiens cDNA clone 247722 3'	
									N54281	zn76c02.s1 Stratagene NT2 neuronal precursor 937230 Homo sapiens cDNA clone 564098 3'	
									AA114075	Homo sapiens guanylate kinase (GUK1) mRNA	
166	CATGTGGAGTGGAGG	H953251	18	15	7	22	48	Examples	L76200	Human mRNA for precursor of apolipoprotein C1	
167	CATGTGCCCCAGGT	H955723	0	3	3	37	4	Examples	X00570	Homo sapiens cathepsin B mRNA	
168	CATGTGGTGAGCCA	H962086	13	15	13	76	27	Examples	L16510	Human cathepsin B proteinase mRNA, complete cds	
									M14221	Human enigma gene	
169	CATGTGTGAGCCCCCT	H975446	3	3	3	22	8	Examples	L35240	Homo sapiens ribosomal protein L34 (RPL34) mRNA	
170	CATGTGTGCTAAATG	H976644	8	21	26	18	50	Examples	L38941	Human gene for histone H1(0).	
171	CATGTGTGTTTGT	H978687	6	7	16	25	15	Examples	X03473	zk23g08.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 471422 3'	
172	CATGTATGGAATCTC	H997944	0	1	1	21	1	Examples	AA034505		

[illegible]

SI	CATGTTTCCTTCCTT	H1038296	0	6	3	7	17	Examples	M20471	Human brain-type clathrin light-chain a mRNA
									M20472	Human lymphocyte clathrin light-chain A mRNA
IS2	CATGTTTGACCTTT	H1041504	2	0	0	16	1	Examples	X78947	H. sapiens mRNA for connective tissue growth factor
									U14750	Human connective tissue growth factor mRNA
IS4	CATGTTTGTAAAA	H1044225							H06492	y178c08.s1 Homo sapiens cDNA clone 44273 3'
									T35952	EST94173 Homo sapiens cDNA 3' end similar to None
									AA253218	zz53g10.s1 Soares NhHMPu S1 Homo sapiens cDNA clone 667170 3'

Table 5 - Transcripts increased in pancreas and colorectal cancer
**SAGE tag that were elevated in both in colorectal and pancreatic tumor,
 and are likely to be specific for tumor in general.**

Tag Sequence	Tag Number	Accession	Description
1 CATG TGAATGAC C	-950498	M10629	Human alpha-1 collagen gene, 3' end with polyA sit
2 CATG CACTCAAGG G	-294155	U42376	Human retinoic acid induced RIG-E precursor (E) mR
		U56145	Human thymic shared antigen-1/stem cell antigen-2
3 CATG ATGTGAAGAG T(A)	-243747	J03040	Human SPARC/osteonectin mRNA, complete cds.
		M25746	Human osteonectin gene exon 10, complete cds.
4 CATG GCCCAAGGAC C	-610466	X53416	Human mRNA for actin-binding protein (filamin) (AB
5 CATG ATCTGTAC T	-229106	X02761	Human mRNA for fibronectin (FN precursor).
		K00799	human fibronectin (fn) 3' coding region and flank,
6 CATG GTGCCTGAG C	-760291	X58536	Human mRNA for HLA class I locus C heavy chain.
		M26432	Human MHC class I HLA-C.1 gene, complete cds.
7 CATG ACAGGCTACG G	-76231	M95787	Human 22kDa smooth muscle protein (SM22) mRNA, com
		M83106	Human SM22 mRNA, 5' end.
8 CATG GTGTGTTGT A	-769020	M77349	Human transforming growth factor-beta induced gene
9 CATG GATTCTCAG C	-589267	X53279	Human mRNA for placental-like alkaline phosphatase
		X55958	H.sapiens mRNA for alkaline phosphatase.
		J04948	Human alkaline phosphatase (ALP-1) mRNA, complete
10 CATG ACCATTCTGC T	-85882	X57351	Human 1-8D gene from interferon-inducible gene fam
		X02490	Human interferon-inducible mRNA (CDNA 1-8).
			Human mRNA for alpha-actinin.
11 CATG TCCTTCTCCA C	-884181	X15804	Human mRNA for KIAA0190 protein.
12 CATG CTTCTGTGTA C,T	-515821	D80012	Human TB2 gene mRNA, 3' end.
13 CATG ATGTAAAAA T	-241665	M74090	Human lysozyme mRNA, complete cds with an Alu repe
		J03801	Human lysozyme mRNA, complete cds.
		M19045	Human mRNA for Nm23 protein, involved in developme
14 CATG GGCAGAGGAC C	-673954	X17620	H.sapiens nm23H1 gene.
		X75598	Human int-6 mRNA, complete cds.
15 CATG AATATTGAGA A	-53129	U62962	Human HepG2 3' region cDNA, clone hmd2c11.
16 CATG TTTTGTATAA A	-1048113	D16891	H.sapiens mRNA for fibulin-1 C.
17 CATG CAGCTGGCCA T	-302741	X53743	

18	CATG GTTCACATTA	G	-774461	X00497	Human mRNA for HLA-DR antigens associated invariant
				M13560	Human Ia-associated invariant gamma-chain gene, ex
19	CATG AAAAGAAACT	T	-2056	Y00345	Human mRNA for polyA binding protein.
20	CATG AATGACGGCA	G	-58533	M61831	Human S-adenosylhomocysteine hydrolase (AHCY) mRNA
				M61832	Human S-adenosylhomocysteine hydrolase (AHCY) mRNA
21	CATG TGAATAAAA	C	-918273	X16934	Human hb23 gene for B23 nucleophosmin.
				M28699	Homo sapiens nucleolar phosphoprotein B23 (NPM1) m
				M23613	Human nucleophosmin mRNA, complete cds.
				M26697	Human nucleolar protein (B23) mRNA, complete cds.
22	CATG TTATGGGATC	T	-998030	M24194	Human MHC protein homologous to chicken B complex
23	CATG CAATAAATGT	T	-274492	D23661	Human mRNA for ribosomal protein L37, complete cds
				L11567	Human mRNA for ribosomal protein L37 mRNA, complete
					Homo sapiens ribosomal protein 2.
24	CATG AGCCTTTGTT	G	-155632	D83174	Human mRNA for collagen binding protein 2.
25	CATG ACCTGTATCC	C	-97078	X57352	Human 1-8U gene from interferon-inducible gene fam
26	CATG TTCAATAAAA	A	-1000193	M17886	Human acidic ribosomal phosphoprotein P1 mRNA, com
				J05068	Human transcobalamin I mRNA, complete cds.
27	CATG CGACCCACG	C	-398663	M12529	Human apolipoprotein E mRNA, complete cds.
				K00396	Human apolipoprotein E (epsilon 2 and 3 alleles) m
28	CATG CAGATCTTTG	T	-298495	X56998	Human Uba52 adrenal mRNA for ubiquitin-52 amino ac
				X56999	Human Uba52 placental mRNA for ubiquitin-52 amino
29	CATG CTGGCGAGCG	C	-501287	X07491	Human DNA inserts showing sperm-specific hypomethy
				M91670	Human ubiquitin carrier protein (E2-EPF) mRNA, com
30	CATG ATTGGCTTAA	A	-256497	L14272	Human prohibitin (PHB) gene, exons 1-7.
				S85655	prohibitin [human, mRNA, 1043 nt].
31	CATG GTGGTGACA	C	-765573	U62435	Human nicotinic acetylcholine receptor alpha6 subu
				U68041	Human breast and ovarian cancer susceptibility pro
32	CATG TCCTGCCCA	T	-883029	M24398	Human parathymosin mRNA, complete cds.
33	CATG ACTGGGTCTA	T	-125661	X58965	H. sapiens RNA for nm23-H2 gene.
				M36981	Human putative NDP kinase (nm23-H2S) mRNA, complet
				L16785	Human putative c-myc transcription factor (puf) mRNA
				U02032	Homo sapiens c-myc transcription factor (puf) mRNA
34	CATG AAGAAGATAG	A	-33331		Human ribosomal protein L23a mRNA, partial cds.
				U37230	Human ribosomal protein L23a mRNA, complete cds.
				U43701	Human ribosomal protein L23a mRNA, complete cds.

				L13799	Homo sapiens (clone 01) liver expressed protein mR
35	CATG ACATCATCGA T	-79065	L06505		Human ribosomal protein L12 mRNA, complete cds.
36	CATG CTGTTGGTGA T	-507577	D14530		Human homolog of yeast ribosomal protein S28, comp
37	CATG ATTATTTTC T	-249854	X57959		H.sapiens mRNA for ribosomal protein L7.
			X57958		H.sapiens mRNA for ribosomal protein L7.
			X52967		Human mRNA for ribosomal protein L7.
			L16558		Human ribosomal protein L7 (RPL7) mRNA, complete c
38	CATG GCTTTTAAGG A	-655115	L06498		Homo sapiens ribosomal protein S20 (RPS20) mRNA, c
39	CATG GGCNAGAAGA A	-672265	L19527		Homo sapiens ribosomal protein L27 (RPL27) mRNA, c
			L25346		Homo sapiens ribosomal protein L27 (homologue of r
40	CATG CTCCTTCGAGA A	-490889	Y00433		Human mRNA for glutathione peroxidase (EC 1.11.1.9
			Y00483		Human gene for glutathione peroxidase.
			X13710		H.sapiens unspliced mRNA for glutathione peroxidase
			X13709		Human gpx1 mRNA for glutathione peroxidase.
			M21304		Human glutathione peroxidase (GPX1) mRNA, complete
41	CATG CTGTTGATTG C	-507455	X04347		Human liver mRNA fragment DNA binding protein UPI
			U00947		Human clone C4E 3.2 (CAC)n/(GTG)n repeat-contains
42	CATG CTGGGTTAAT A	-502724	M81757		H.sapiens S19 ribosomal protein mRNA, complete cds
43	CATG ATGGCTGGTA T	-239533	X17206		Human mRNA for LLRep3.
44	CATG GATGCTGCCA A	-583573	X59357		Human mRNA for Epstein-Barr virus small RNAs (EBER
			L21756		Homo sapiens acute myeloid leukemia associated pro
			D17652		Human mRNA for HBp15/L22, complete cds.
			S76343		AML1...EAP (translocation breakpoint) [human, chro
45	CATG CCTTCGAGAT C	-390692	U14970		Human ribosomal protein S5 mRNA, complete cds.
46	CATG CTCCTCACCT G	-482584	U16811		Human Bak mRNA, complete cds.
			U23765		Human Bak protein mRNA, complete cds.
47	CATG TGTGTTGAGA G	-978825	X16869		Human mRNA for elongation factor 1-alpha (clone CE
			X16872		Human DNA for elongation factor 1-alpha (clone lam
			X03558		Human mRNA for elongation factor 1 alpha subunit (
			D17182		Human HepG2 3' region MboI cDNA, clone hmd2h03m3.
			D17245		Human HepG2 3' region MboI cDNA, clone hmd4h05m3.
			D17259		Human HepG2 3' region MboI cDNA, clone hmd5d07m3.
			D17276		Human HepG2 3' region MboI cDNA, clone hmd6a12m3.

			M27364	Human elongation factor 1 alpha mRNA, 3' end.
			M29548	Human elongation factor 1-alpha (EF1A) mRNA, parti
			L41490	Homo sapiens oncogene PTI-1 mRNA, complete cds.
			L41498	Homo sapiens oncogene PTI-1 mRNA, complete cds.
			U57846	Human ribosomal protein L39 mRNA, complete cds.
48	CATG TTACCATATC	A	-988366	H.sapiens GPx-4 mRNA for phospholipid hydroperoxid
49	CATG GCTGCTGGG	C	-621035	H.sapiens gene for ribosomal protein L38.
50	CATG CCTCGGARA	T	-383489	H.sapiens mRNA for ribosomal protein L6.
51	CATG TACAGAGGA	A	-803369	Human mRNA for DNA-binding protein, TAXREB107, com
			-803369	neoplasm-related C140 product [human, thyroid carc
			-803369	Human beta-tubulin pseudogene.
52	CATG AACGACCTCG	T	-24951	Human mRNA fragment encoding beta-tubulin. (from c
			-24951	Human mRNA for neurite outgrowth-promoting protein
53	CATG CCCTGCCTTG	T	-358783	Human stimulator of TAR RNA binding (SRB) mRNA, co
54	CATG CCCAGGGAGA	A	-346761	Human HepG2 3' region cDNA, clone hmd4f11.
			D16933	H.sapiens mRNA for elongation factor 2.
55	CATG AGCAGCTCCA	G	-148949	H.sapiens HRPL4 mRNA.
56	CATG CGCCGAACA	C	-416261	Human mRNA for ribosomal protein, complete cds.
			D23660	Human 26-kDa cell surface protein TAPA-1 mRNA, com
57	CATG CTAAAAAAA	A	-458753	Human glycyl-tRNA synthetase mRNA, complete cds.
58	CATG GGCTGATGTG	G	-686319	Human glycyl-tRNA synthetase mRNA, complete cds.
			U09587	Human T-cell mRNA for glycyl tRNA synthetase, comp
			D30558	Human mRNA for HL23 ribosomal protein L17.
59	CATG ATTCTCCAGT	A	-253260	Human mRNA for ribosomal protein L17.
			X52839	H.sapiens mRNA for laminin-binding protein.
60	CATG GAAAAATGGT	T	-524524	Human 37 kD laminin receptor precursor/p40 ribosom
			X15005	Human colin carcinoma laminin-binding protein mRNA
			U43901	Human laminin receptor (2H5 epitope) mRNA, 5' end.
			J03799	Human mRNA for ribosomal protein L14, complete cds
61	CATG CAGCTCACTG	A	-302367	Human (clone CTG-B33) mRNA sequence.
			L10376	CAG-isl 7 (trinucleotide repeat-containing sequenc
			S80520	Human ribosomal protein S29 mRNA, complete cds.
62	CATG ATAATTCTTT	G	-200576	Human ribosomal protein S29 mRNA, complete cds.

63	CATG AATCCTGTGG	A	-55227	L31610	Homo sapiens (clone cori-1c15) S29 ribosomal prote
64	CATG AATAGGTCCA	A	-51925	M64716	H.sapiens mRNA for ribosomal protein L8.
					Human ribosomal protein S25 mRNA, complete cds.
65	CATG AAAAAAAAAA	A (C, G,T)	-1	X83412	H.sapiens B1 mRNA for mucin.
				Z32564	H.sapiens FRGAMMA mRNA (819bp) for folate receptor
				Z32633	H.sapiens FRGAMMA' mRNA for folate receptor [817bp
				X76180	H.sapiens mRNA for lung amiloride sensitive Na+ ch
				U08470	Human FR-gamma' mRNA, complete cds.
				U08471	Human folate receptor 3 mRNA, complete cds.
				U48697	Human mariner-like element-containing mRNA, clone
				D28532	Human mRNA for renal Na+-dependent phosphate cotra
				M55914	Human c-myc binding protein (MBP-1) mRNA, complete
				L06175	Homo Sapiens P5-1 mRNA, complete cds.
				S73775	calmitine-mitochondrial calcium-binding protein [h
				S77393	transcript chi38 [human, RFL, RF48 stomach cancer c
				X60036	H.sapiens mRNA for mitochondrial phosphate carrier
66	CATG CCAGAACACA	C	-335945	X79238	H.sapiens mRNA for ribosomal protein L30.
				L16991	H.sapiens mRNA for ribosomal protein L30.
67	CATG AAGGTGGAGG	A	-44683	X80822	Human thymidylate kinase (CDC8) mRNA, complete cds
68	CATG CCTAGCTGGA	T	-379369	X52856	H.sapiens mRNA for ORF.
				X52857	Human cyclophilin-related processed pseudogene.
				X52854	Human cyclophilin-related processed pseudogene.
				X52851	Human cyclophilin-related processed pseudogene.
				Y00052	Human cyclophilin gene for cyclophilin (EC 5.2.1.8
					Human mRNA for T-cell cyclophilin.
69	CATG GAACACATCC	A	-528694	X63527	H.sapiens mRNA for ribosomal protein L19.
				S56985	ribosomal protein L19 [human, breast cancer cell 1
70	CATG AAGGAGATGG	G	-41531	X69181	H.sapiens mRNA for ribosomal protein L31.
				X15940	Human mRNA for ribosomal protein L31.
71	CATG AGGCTACGGA	A	-171113	Z29650	H.sapiens SMCX mRNA.
				D17233	Human HepG2 3' region MboI cDNA, clone hmd4c12m3.
72	CATG AGGTCCTAGC	C	-177610	X08096	Human GST pi gene for glutathione S-transferase pi

			X06547	Human mRNA for class Pi glutathione S-transferase
			X15480	Human mRNA for anionic glutathione-S-transferase (
			X08058	Human glutathione S-transferase pi gene.
			U12472	Human glutathione S-transferase (GST phi) gene, co
			U21689	Human glutathione S-transferase-P1c gene, complete
			U62589	Human glutathione S-transferase P1c (GSTp1c) mRNA,
			M69113	Human fatty acid ethyl ester synthase-III mRNA seq
			M24485	Homo sapiens (clone pHGST-pi) glutathione S-transf
			X69150	H. sapiens mRNA for ribosomal protein S18.
73	CATG TGGTGTGAG G	-965603	M96153	H. sapiens apolipoprotein B gene sequence.
			L06432	Homo sapiens 18S ribosomal protein (HKE3) mRNA seq
			M17885	Homo sapiens 18S ribosomal phosphoprotein P0 mRNA, com
74	CATG CTCACATCT C	-475448	L25899	Human acidic ribosomal phosphoprotein L10 mRNA, complete cds.
75	CATG GTGTTAACCA G	-769045	X58125	Human ribosomal protein L10 mRNA, complete cds.
76	CATG AGGCTTCCA A	-174037	D17268	Human (D9S55) DNA segment containing (TG)24 repeat
			M73791	Human HepG2 3' region MboI cDNA, clone hmd5h09m3.
			M64241	Human novel gene mRNA, complete cds.
			S35960	Human Wilm's tumor-related protein (QM) mRNA, comp
			M17887	laminin receptor homolog (3' region) (human, mRNA
77	CATG GGATTGGCC T	-671654	M11147	Human acidic ribosomal phosphoprotein P2 mRNA, com
			M12938	Human ferritin L chain mRNA, complete cds.
			M10119	Human ferritin light subunit mRNA, partial cds.
			X04409	Human ferritin light subunit mRNA, complete cds.
78	CATG ATTAACAAAG C	-246019	X04408	Human mRNA for coupling protein G(s) alpha-subunit
			X56009	Human mRNA for coupling protein G(s) alpha subunit
			X07036	Human GSA mRNA for alpha subunit of GsGTP binding
			M21142	Human mRNA stimulatory GTP-binding protein alpha s
			M14631	Human guanine nucleotide-binding protein alpha-sub
			X69173	Human guanine nucleotide-binding protein G-s, alph
79	CATG TGTAACCTGTA A	-968173	K00558	Human alpha-tubulin mRNA, complete cds.
			X56494	Human alpha-tubulin mRNA, complete cds.
80	CATG TGGCCCCCACC C	-955718	M23725	H. sapiens M gene for M1-type and M2-type pyruvate
			M26252	Human M2-type pyruvate kinase mRNA, complete cds.
				Human TCB gene encoding cytosolic thyroid hormone-

81	CATG TAATAAAGGT	G	-798764	X67247	H.sapiens rps8 gene for ribosomal protein S8.
82	CATG GCATAATAGG	T	-602315	X89401	H.sapiens mRNA for large subunit of ribosomal prot
				U14967	Human ribosomal protein L21 mRNA, complete cds.
				U25789	Human ribosomal protein L21 mRNA, complete cds.
				L38826	Homo sapiens L21 ribosomal protein gene, partial c
83	CATG TACCATCAAT	A	-807748	X53778	H.sapiens hng mRNA for uracil DNA glycosylase.
				U34995	Human normal keratinocyte subtraction library mRN
				J02642	Human glyceraldehyde 3-phosphate dehydrogenase mRN
				M36164	Human glyceraldehyde-3-phosphate dehydrogenase mRN
				M33197	Human glyceraldehyde-3-phosphate dehydrogenase (GA
84	CATG ATTTGTCCCA	G	-260949	X14957	Human hmgI mRNA for high mobility group protein I.
				X14958	Human hmgI mRNA for high mobility group protein Y.
				M23614	Human HMG-I protein isoform mRNA (HMG1 gene), clon
				M23619	Human HMG-I protein isoform mRNA (HMG1 gene), clon
				L17131	Human high mobility group protein (HMG-I(Y)) gene
				M23615	Human HMG-Y protein isoform mRNA (HMG1 gene), clon
				M23616	Human HMG-Y protein isoform mRNA (HMG1 gene), clon
				M23617	Human HMG-Y protein isoform mRNA (HMG1 gene), clon
				M23618	Human HMG-Y protein isoform mRNA (HMG1 gene), clon
85	CATG GAGGGAGTTT	C	-567488	U14968	Human ribosomal protein L27a mRNA, complete cds.
86	CATG CGCCGCCGGC	T	-416106	U12465	Human ribosomal protein L35 mRNA, complete cds.
87	CATG GTGAACCCCA	ALL	-753749	Z63072	H.sapiens CpG island DNA genomic MseI fragment, cl
88	CATG GTGAACCCCA	ALL	-753749	X16294	Human repetitive DNA containing interspersed repea
89	CATG AAGACAGTGG	C	-33979	X66699	H.sapiens mRNA for ribosomal protein L37a.
				L06499	Homo sapiens ribosomal protein L37a (RPL37A) mRNA,
				L22154	Human ribosomal protein L37a mRNA sequence.
90	CATG CCCAGCCAG	T	-348755	X55715	Human Hums3 mRNA for 40S ribosomal protein s3.
				U14990	Human XP1PO ribosomal protein S3 (rps3) mRNA, comp
				U14991	Human XP2NE ribosomal protein S3 (rps3) mRNA, comp
				U14992	Human IMR-90 ribosomal protein S3 (rps3) mRNA, com
				S42658	S3 ribosomal protein [human, colon, mRNA, 826 nt].
91	CATG TGGCAAGC	C	-959498	X63526	H.sapiens mRNA for protein homologous to elongatio
				Z11531	H.sapiens mRNA for elongation factor-1-gamma.

				M55409	Human pancreatic tumor-related protein mRNA, 3' en
92	CATG TGAGGGAATA	A	-928269	M10036	Human triosephosphate isomerase mRNA, complete cds
93	CATG GACGACACGA	G	-549145	U58682	Human ribosomal protein S28 mRNA, complete cds.
				M58458	Human ribosomal protein S4 (RPS4X) isoform mRNA, c
				M22146	Human scar protein mRNA, complete cds.
94	CATG AACGGGCCA	A	-26261	Z23063	Homo sapiens macrophage migration inhibitory facto
				L10612	Human glycosylation-inhibiting factor mRNA, comple
				M95775	Homo sapiens macrophage migration inhibitory facto
				L19686	Homo sapiens macrophage migration inhibitory facto
				M25639	Human migration inhibitory factor (MIF) mRNA, comp
					Human mRNA for ribosomal protein L32.
95	CATG TGCACGTTT	C	-935680	X03342	Human mRNA from chromosome 15 gene with homology t
				K03002	Human mRNA from chromosome 15 gene with homology t
96	CATG CACAAACGGT	A	-278636	U57847	Human ribosomal protein S27 mRNA, complete cds.
				L19739	Homo sapiens metallopeptidase (MPS1) mRNA, compl
97	CATG GGAGTGACA	T	-667269	L11566	Homo sapiens ribosomal protein L18 (RPL18) mRNA, c
98	CATG GCCGAGGAAG	G	-615043	Z54999	H.sapiens CpG island DNA genomic MseI fragment, cl
				Z57572	H.sapiens CpG island DNA genomic MseI fragment, cl
				Z56073	H.sapiens CpG island DNA genomic MseI fragment, cl
				X53505	Human mRNA for ribosomal protein S12.
99	CATG GGGGAATCG	C	-696375	M92381	Human thymosin beta 10 mRNA, complete cds.
				M20259	Human thymosin beta-10 mRNA, complete cds.
100	CATG GCAGCCATCC	G	-599350	U14969	Human ribosomal protein L28 mRNA, complete cds.
				D17257	Human HepG2 3' region MboI cDNA, clone hmd5d04m3.
101	CATG TAAGGAGCTG	A	-796831	X77770	H.sapiens RPS26 mRNA.
				X69654	H.sapiens mRNA for ribosomal protein S26.
102	CATG GCGAAGCCCC	A	-672342	U12404	Human Csa-19 mRNA, complete cds.
				X79239	H.sapiens mRNA for ribosomal protein S13.
				L01124	Human ribosomal protein S13 (RPS13) mRNA, complete
103	CATG GTTCCCTGCC	C	-775658	X65923	H.sapiens fau mRNA.
				U02523	Human FAU1P pseudogene, trinucleotide repeat regio
104	CATG CCGTCCAAGG	G	-374027	M60854	Human ribosomal protein S16 mRNA, complete cds.
	CATG TTGTCCTCT	G	-1027448	Z12962	H.sapiens mRNA for homologue to yeast ribosomal pr
				S64030	L41 ribosomal protein homologue (clone 7B6) [human,

105	CATG CAAACCATCC	A	-263478	X12883	Human mRNA for cytokeratin 18.
				X12876	Human mRNA fragment for cytokeratin 18.
				X12881	Human mRNA for cytokeratin 18.
				M24842	Human keratin 18 (K18) gene, complete cds.
				M26325	Human cytokeratin 18 mRNA, 3' end.
				M26326	Human keratin 18 mRNA, complete cds.
				M26327	Human cytokeratin 18 mRNA, 3' end.
					Human L23 mRNA for putative ribosomal protein.
106	CATG AGCTCTCCCT	G	-161624	X53777	Human male bone marrow myeloblast mRNA for KIAA022
107	CATG AGGTCAGGAG	A(T)	-177315	D86979	Human DNA for Alu element PIN6.
				X55923	H.sapiens ALU repeat, 230bp.
				X79699	Human mRNA for HLA class II DR-beta (HLA-DR B).
				X12544	H.sapiens flow-sorted chromosome 6 HindIII fragmen
				Z77989	Human clone 2102V-I chromosome 18p telomeric seque
				U11831	Human Alu repeat sequence A3.
				U12580	Human Alu repeat sequence B2.
				U12582	Human Alu repeat sequence D1.
				U12583	Human Alu-Sb2 repeat, clone HALUSB08.
				U14694	Human Alu-Sb2 repeat, clone HALUSB15.
				U14695	Human Alu-Sb2 repeat, clone HALUSB27.
				U14696	Human Alu-Sb2 repeat, clone HUM-11.
				U14697	Human Alu-Sb2 repeat, clone HSB-8P.
				U14698	Human Alu-Sb2 repeat, clone HUM-9.
				U14699	Human Alu-Sb2 repeat, clone HALUSB35.
				U14700	Human Alu-Sb2 repeat, clone HSB-2P.
				U14701	Human Alu-Sb2 repeat, clone HUM-3.
				U14704	Human Alu-Sb2 repeat, clone HUM-10.
				U14706	Human Alu-Sb2 repeat, clone HUM-7.
				U14707	Human (Lawn) c-myc proto-oncogene, complete coding
				J00120	Homo sapiens platelet/endothelial cell adhesion mo
				L34653	Human XV2c gene.
				M37521	NF1-neurofibromatosis type 1 (deletion breakpoint,
				S61789	phosphorylase kinase catalytic subunit PHKG2 homol
				S73483	

			S75201	cholinesterase (Alu element) [human, Insertion Mut
			S75337	(Y Alu polymorphism, YAP, polymorphic subfamily-3)
108	CATG GGGCTGGGT C	-695980	Z49148	H.sapiens mRNA for ribosomal protein L29.
			U10248	Human ribosomal protein L29 (humrpl29) mRNA, compl
			U49083	Human cell surface heparin binding protein HIP mRNA
			D16992	Human HepG2 partial cDNA, clone hmd2d02m5.
			D16911	Human HepG2 3' region cDNA, clone hmd3b09.
			J03537	Human ribosomal protein S6 mRNA, complete cds.
			M20020	Human ribosomal protein S6 mRNA, complete cds.
				EST
109	CATG ACGTCTCTT C	-114144		EST
110	CATG TCTCCATACC C	-906438		EST
111	CATG GACTGCGTGC C	-555450		EST
112	CATG CTTAATCCTG A	-508767		EST
113	CATG GGTGGCAGG G	-719435		EST
114	CATG GCCCTCTGCC A	-613862		EST
115	CATG AACAGAAGCA A	-18469		EST
116	CATG CTGCCGAGCT C	-497192		EST
117	CATG TTCCTCGGC A	-1007018		EST
118	CATG AACTAATACT A	-28872		EST
119	CATG TAGATAATGG C	-822331		EST
120	CATG GCACACCCC A,C	-607318		EST
121	CATG GAACCCCTGG A	-529899		EST
122	CATG AACTAARAA A	-28673		EST
123	CATG GAATGTAG A	-528067		EST
124	CATG ACTCCAAAA A	-119809		EST
125	CATG GTTCGTGCC A	-777109		EST
126	CATG TTACCTCCTT C	-989024		EST
127	CATG GCACAAGAG A	-594051		EST
128	CATG CCCTGGGTTT C	-359102		EST
129	CATG GCCTGTATGA G	-621369		EST
130	CATG CCCGTCGGA A	-355689		EST
131	CATG AGGAAGCTG C	-163999		EST
132	CATG TCAGATCTTT G	-861056		EST

EST
EST
EST
EST

133	CATG	CCAGGAGGAA	T	-338081
134	CATG	TCACCCACAC	C	-857362
135	CATG	GTGTTGCACA	A	-769605
136	CATG	GCCGTGTCCG	C	-618199

Isolation of partial cDNA (3' fragment) by 3' directed PCR reaction

This procedure is a modification of the protocol described in Polyak et al. (1997) Nature 389:300. Briefly, the procedure uses SAGE tags in PCR reaction such that the resultant PCR product contains the SAGE tag of interest as well as additional cDNA, the length of which is defined by the position of the tag with respect to the 3' end of the cDNA. The cDNA product derived from such a transcript driven PCR reaction can be used for many applications.

RNA from a source believed to express the cDNA corresponding to a given tag is first converted to double-stranded cDNA using any standard cDNA protocol. Similar conditions used to generate cDNA for SAGE library construction can be employed except that a modified oligo-dT primer is used to drive the first strand synthesis. For example, the oligonucleotide of composition 5'-B-TCC GGC GCG CCG TTT T CC CAG TCA CGA(30)-3', contains a poly-T stretch at the 3' end for hybridization and priming from poly-A tails, an M13 priming site for use in subsequent PCR steps, a 5' Biotin label (B) for capture to streptavidin-coated magnetic beads, and an AscI restriction endonuclease site for releasing the cDNA from the streptavidin-coated magnetic beads. Theoretically, any sufficiently-sized DNA region capable of hybridizing to a PCR primer can be used as well as any other 8 base pair recognizing endonuclease.

cDNA constructed utilizing this or similar modified oligo-dT primer is then processed exactly as described in U.S. Patent No. (insert) up until adapter ligation where only one adapter is ligated to the cDNA pool. After adapter ligation, the cDNA is released from the streptavidin-coated magnetic beads and is then used as a template for cDNA amplification.

Various PCR protocols can be employed using PCR priming sites within the 3' modified oligo-dT primer and the SAGE tag. The SAGE tag-derived PCR primer employed can be of varying length dictated by 5' extension of the tag into the adaptor sequence. cDNA products are now available for a variety of applications.

This technique can be further modified by: (1) altering the length and/or content of the modified oligo-dT primer; (2) ligating adaptors other than that previously employed within the SAGE protocol; (3) performing PCR from template retained on the streptavidin-coated magnetic beads; and (4) priming first strand cDNA synthesis with non-oligo-dT based primers.

Isolation of cDNA using GeneTrapper or modified GeneTrapper Technology

The reagents and manufacturer's instructions for this technology are commercially available from Life Technologies, Inc., Gaithersburg, Maryland. Briefly, a complex population of single-stranded phagemid DNA containing directional cDNA inserts is enriched for the target sequence by hybridization in solution to a biotinylated oligonucleotide probe complementary to the target sequence. The hybrids are captured on streptavidin-coated paramagnetic beads. A magnet retrieves the paramagnetic beads from the solution, leaving nonhybridized single-stranded DNAs behind. Subsequently, the captured single-stranded DNA target is released from the biotinylated oligonucleotide. After release, the cDNA clone is further enriched by using a nonbiotinylated target oligonucleotide to specifically prime conversion of the single-stranded target to double-stranded DNA. Following transformation and plating, typically 20% to 100% of the colonies represent the cDNA clone of interest. To identify the desired cDNA clone, the colonies may be screened by colony hybridization using the ³²P-labeled oligonucleotide as described above for solution hybridization, or alternatively by DNA sequencing and alignment of all sequences obtained from numerous clones to determine a consensus sequence.

The genes which are identified herein as being differentially expressed in normal and cancer cells can be used diagnostically and prognostically. Transcription levels in a test sample suspected of being neoplastic can be determined and compared to the levels in normal colon cells. The test sample may be from any tissue suspected of neoplasia, and particularly from either suspected colorectal or suspected pancreatic cancer cells. The control cells for

the purposes of comparison are normal cells, preferably of the same tissue type as the test sample, *e.g.*, colon cells, or pancreatic duct epithelial cells. Upregulation of transcription or downregulation of transcription is therefore diagnostic of the neoplastic state, depending on what gene is used as a test reagent. Similarly, transcription levels can be monitored to assess patient responses to anti-tumor therapies. Transcription levels will also provide prognostic information. For example, the level of transcription in a test sample can be compared to levels found in *bona fide* normal and tumor cells. More extreme deviations from normal expression levels indicate a poorer prognosis.

Transcription levels can be determined according to any means known in the art. These include, without limitation, Northern blots, nuclear run-on assays, *in vitro* transcription assays, primer extension assays, quantitative reverse transcriptase-polymerase chain reactions (RT-PCR), and hybrid filter binding assays. These techniques are well known in the art. See J.C. Alwine, D.J. Kemp, G.R. Stark, *Proc. Natl. Acad. Sci. U.S.A.* 74, 5350 (1977); K. Zinn, D. Di-Maio, T. Maniatis, *Cell* 34, 865 (1983); G. Veres, R.A. Gibbs, S.E. Scherer, C.T. Caskey, *Science* 237, 415 (1987).

Similarly, upregulated genes and downregulated genes can be detected by measuring expression of their protein products. This can be done by any means known in the art, including but not limited to Western (immuno) blot, enzyme linked immunoadsorbent assay, radioimmunoassay, and enzyme assay. Such techniques are well known in the art. Protein products can be detected in tissue samples of a test patient, using a suspect sample as a test sample, and a matched normal tissue sample from the same tissue type as a control. If normal tissue is not available then a closely related tissue type can be used. Desirably both the samples being compared will be from the same individual. Alternatively, aberrant expression levels of protein products can be detected in body samples, such as blood, serum, feces, urine, sputum. As a control, a normal matched sample can be used from a healthy individual. Aberrant expression levels of transcripts can also be detected in such body samples, particularly in blood and serum.

Probes for use in the assays for transcription levels of particular genes or sets of genes may be RNA or DNA. The probes will be isolated substantially free of other cellular RNAs or DNAs. If the reagent contains one probe then it will comprise at least 50% of the nucleic acids in the reagent composition. If the reagent contains more than one probe, then the proportion will decrease accordingly, so that specific probes will still comprise at least 50% of the nucleic acids in the reagent composition.

Probes can be labeled according to any means known in the art. These may include radioactive labels, fluorescent labels, enzymatic labels, and binding partner labels such as biotin. Means for labeling and detecting probes are well known in the art. Probes comprise at least 10, 11, 12, 15, 20, or 30 contiguous nucleotides of a selected gene.

This invention provides proteins or polypeptides expressed from the polynucleotides of this invention, which is intended to include wild-type and recombinantly produced polypeptides and proteins from procaryotic and eucaryotic host cells, as well as muteins, analogs and fragments thereof. In some embodiments, the term also includes antibodies and anti-idiotypic antibodies.

It is understood that functional equivalents or variants of the wild-type polypeptide or protein also are within the scope of this invention, for example, those having conservative amino acid substitutions. Other analogs include fusion proteins comprising a protein or polypeptide.

The proteins and polypeptides of this invention are obtainable by a number of processes well known to those of skill in the art, which include purification, chemical synthesis and recombinant methods. Full length proteins can be purified from a colon or pancreatic cell or tissue lysate by methods such as immunoprecipitation with antibody, and standard techniques such as gel filtration, ion-exchange, reversed-phase, and affinity chromatography using a fusion protein as shown herein. For such methodology, see for example Deutscher et al. (1999) Guide To Protein Purification: Methods In Enzymology (Vol. 182, Academic Press). Accordingly, this invention also

provides the processes for obtaining these proteins and polypeptides as well as the products obtainable and obtained by these processes.

The proteins and polypeptides also can be obtained by chemical synthesis using a commercially available automated peptide synthesizer such as those manufactured by Perkin Elmer/Applied Biosystems, Inc., Model 430A or 431A, Foster City. The synthesized protein or polypeptide can be precipitated and further purified, for example by high performance liquid chromatography (HPLC). Accordingly, this invention also provides a process for chemically synthesizing the proteins of this invention by providing the sequence of the protein and reagents, such as amino acids and enzymes and linking together the amino acids in the proper orientation and linear sequence.

Alternatively, the proteins and polypeptides can be obtained by well-known recombinant methods as described, for example, in Sambrook et al., (1989), *supra*, using the host cell and vector systems described above.

Also provided by this application are the polypeptides and proteins described herein conjugated to a detectable agent for use in the diagnostic methods. For example, detectably labeled proteins and polypeptides can be bound to a column and used for the detection and purification of antibodies. They also are useful as immunogens for the production of antibodies as described below. The proteins and fragments of this invention are useful in an *in vitro* assay system to screen for agents or drugs, which modulate cellular processes.

The proteins of this invention also can be combined with various liquid phase carriers, such as sterile or aqueous solutions, pharmaceutically acceptable carriers, suspensions and emulsions. Examples of non-aqueous solvents include propyl ethylene glycol, polyethylene glycol and vegetable oils. When used to prepare antibodies, the carriers also can include an adjuvant that is useful to non-specifically augment a specific immune response. A skilled artisan can easily determine whether an adjuvant is required and select one. However, for the purpose of illustration only, suitable adjuvants include, but

are not limited to Freund's Complete and Incomplete, mineral salts and polynucleotides.

This invention also provides a pharmaceutical composition comprising any of a protein, analog, mutein, polypeptide fragment, antibody, antibody
5 fragment or anti-idiotypic antibody of this invention, alone or in combination with each other or other agents, and an acceptable carrier. These compositions are useful for various diagnostic and therapeutic methods.

Antibodies can be generated using the proteins encoded by the transcripts identified by the tags disclosed herein. Use of all or portions of the
10 protein as immunogens is routine in the art. Similarly, fusion proteins can be used as immunogens. Antibodies can be affinity purified using the proteins or portions thereof used as immunogens. Similarly, monoclonal antibodies specifically immunoreactive with the protein sequences of the invention can be generated according to techniques which are well known in the art.

Antibodies can be used analytically to quantitate the expression of particular transcripts identified herein as upregulated or downregulated in cancer. In addition, antibodies can be conjugated or non-covalently linked to cytotoxic agents, such as cytotoxins, radionuclides, chemotherapeutic drugs, etc. Such antibodies can be used therapeutically to specifically target cancer
15 cells in which the protein antigens are upregulated. These include the proteins encoded by the transcripts identified by the tags shown in Tables 2, 4, and 5. Means of making such linked cytotoxic antibodies and of administering the same are well known in the art.

Also provided by this invention is an antibody capable of specifically
25 forming a complex with the proteins or polypeptides as described above. The term "antibody" includes polyclonal antibodies and monoclonal antibodies. The antibodies include, but are not limited to mouse, rat, and rabbit or human antibodies.

Laboratory methods for producing polyclonal antibodies and
30 monoclonal antibodies, as well as deducing their corresponding nucleic acid sequences, are known in the art, see Harlow and Lane (1988) supra and

Sambrook et al. (1989) supra. The monoclonal antibodies of this invention can be biologically produced by introducing protein or a fragment thereof into an animal, e.g., a mouse or a rabbit. The antibody producing cells in the animal are isolated and fused with myeloma cells or heteromyeloma cells to produce hybrid cells or hybridomas. Accordingly, the hybridoma cells producing the monoclonal antibodies of this invention also are provided.

Thus, using the protein or fragment thereof, and well known methods, one of skill in the art can produce and screen the hybridoma cells and antibodies of this invention for antibodies having the ability to bind the proteins or polypeptides.

If a monoclonal antibody being tested binds with the protein or polypeptide, then the antibody being tested and the antibodies provided by the hybridomas of this invention are equivalent. It also is possible to determine without undue experimentation, whether an antibody has the same specificity as the monoclonal antibody of this invention by determining whether the antibody being tested prevents a monoclonal antibody of this invention from binding the protein or polypeptide with which the monoclonal antibody is normally reactive. If the antibody being tested competes with the monoclonal antibody of the invention as shown by a decrease in binding by the monoclonal antibody of this invention, then it is likely that the two antibodies bind to the same or a closely related epitope. Alternatively, one can pre-incubate the monoclonal antibody of this invention with a protein with which it is normally reactive, and determine if the monoclonal antibody being tested is inhibited in its ability to bind the antigen. If the monoclonal antibody being tested is inhibited then, in all likelihood, it has the same, or a closely related, epitopic specificity as the monoclonal antibody of this invention.

The term "antibody" also is intended to include antibodies of all isotypes. Particular isotypes of a monoclonal antibody can be prepared either directly by selecting from the initial fusion, or prepared secondarily, from a parental hybridoma secreting a monoclonal antibody of different isotype by using the sib selection technique to isolate class switch variants using the

procedure described in Steplewski et al. (1985) Proc. Natl. Acad. Sci. 82:8653 or Spira et al. (1984) J. Immunol. Methods 74:307.

This invention also provides biological active fragments of the polyclonal and monoclonal antibodies described above. These "antibody fragments" retain some ability to selectively bind with its antigen or immunogen. Such antibody fragments can include, but are not limited to:

- (1) Fab,
- (2) Fab',
- (3) F(ab')₂,
- (4) Fv, and
- (5) SCA

A specific example of "a biologically active antibody fragment" is a CDR region of the antibody. Methods of making these fragments are known in the art, see for example, Harlow and Lane, (1988) supra.

The antibodies of this invention also can be modified to create chimeric antibodies and humanized antibodies (Oi, et al. (1986) BioTechniques 4(3):214). Chimeric antibodies are those in which the various domains of the antibodies' heavy and light chains are coded for by DNA from more than one species.

The isolation of other hybridomas secreting monoclonal antibodies with the specificity of the monoclonal antibodies of the invention can also be accomplished by one of ordinary skill in the art by producing anti-idiotypic antibodies (Herlyn, et al. (1986) Science 232:100). An anti-idiotypic antibody is an antibody which recognizes unique determinants present on the monoclonal antibody produced by the hybridoma of interest.

Idiotypic identity between monoclonal antibodies of two hybridomas demonstrates that the two monoclonal antibodies are the same with respect to their recognition of the same epitopic determinant. Thus, by using antibodies to the epitopic determinants on a monoclonal antibody it is possible to identify other hybridomas expressing monoclonal antibodies of the same epitopic specificity.

It is also possible to use the anti-idiotypic technology to produce monoclonal antibodies which mimic an epitope. For example, an anti-idiotypic monoclonal antibody made to a first monoclonal antibody will have a binding domain in the hypervariable region which is the mirror image of the epitope bound by the first monoclonal antibody. Thus, in this instance, the anti-idiotypic monoclonal antibody could be used for immunization for production of these antibodies.

As used in this invention, the term "epitope" is meant to include any determinant having specific affinity for the monoclonal antibodies of the invention. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics.

The antibodies of this invention can be linked to a detectable agent or label. There are many different labels and methods of labeling known to those of ordinary skill in the art.

The antibody-label complex is useful to detect the protein or fragments in a sample, using standard immunochemical techniques such as immunohistochemistry as described by Harlow and Lane (1988) *supra*. Competitive and non-competitive immunoassays in either a direct or indirect format are examples of such assays, e.g., enzyme linked immunoassay (ELISA) radioimmunoassay (RIA) and the sandwich (immunometric) assay. Those of skill in the art will know, or can readily discern, other immunoassay formats without undue experimentation.

The coupling of antibodies to low molecular weight haptens can increase the sensitivity of the assay. The haptens can then be specifically detected by means of a second reaction. For example, it is common to use haptens such as biotin, which reacts avidin, or dinitrophenyl, pyridoxal, and fluorescein, which can react with specific anti-hapten antibodies. See Harlow and Lane (1988) *supra*.

The monoclonal antibodies of the invention also can be bound to many different carriers. Thus, this invention also provides compositions containing the antibodies and another substance, active or inert. Examples of well-known carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, agaroses and magnetite. The nature of the carrier can be either soluble or insoluble for purposes of the invention. Those skilled in the art will know of other suitable carriers for binding monoclonal antibodies, or will be able to ascertain such, using routine experimentation.

Compositions containing the antibodies, fragments thereof or cell lines which produce the antibodies, are encompassed by this invention. When these compositions are to be used pharmaceutically, they are combined with a pharmaceutically acceptable carrier.

The present invention also provides a screen for various agents which modulate the expression of a gene in a pancreatic or colon cell. To practice the method in vitro, suitable cell cultures or tissue cultures are first provided. The cell can be a cultured cell or a genetically modified cell in which a transcript from SEQ ID NOS:1-732, or their complements, is expressed. Alternatively, the cells can be from a tissue biopsy. The cells are cultured under conditions (temperature, growth or culture medium and gas (CO₂)) and for an appropriate amount of time to attain exponential proliferation without density dependent constraints. It also is desirable to maintain an additional separate cell culture; one which does not receive the agent being tested as a control.

As is apparent to one of skill in the art, suitable cells may be cultured in microtiter plates and several agents may be assayed at the same time by noting genotypic changes, phenotypic changes or cell death.

When the agent is a composition other than a DNA or RNA, the agent may be directly added to the cell culture or added to culture medium for addition. As is apparent to those skilled in the art, an "effective" amount must be added which can be empirically determined. When the agent is a polynucleotide, it may be directly added by use of a gene gun or

electroporation. Alternatively, it may be inserted into the cell using a gene delivery vehicle or vector as described above.

An agent is a potential therapeutic if it alters the expression of gene in the cell. Altered expression can be detected by assaying for altered mRNA expression or protein expression using the probes, primers and antibodies as described herein.

For the purposes of this invention, an "agent" is intended to include, but not be limited to a biological or chemical compound such as a simple or complex organic or inorganic molecule, a peptide, a protein (e.g. antibody) or a polynucleotide (e.g. anti-sense). A vast array of compounds can be synthesized, for example polymers, such as polypeptides and polynucleotides, and synthetic organic compounds based on various core structures, and these are also included in the term "agent". In addition, various natural sources can provide compounds for screening, such as plant or animal extracts, and the like. It should be understood, although not always explicitly stated that the agent is used alone or in combination with another agent, having the same or different biological activity as the agents identified by the inventive screen. The agents and methods also are intended to be combined with other therapies.

The above disclosure generally describes the present invention. A more complete understanding can be obtained by reference to the following specific examples which are provided herein for purposes of illustration only, and are not intended to limit the scope of the invention.

EXAMPLE 1

This example demonstrates the characterization of the general transcription of human colorectal epithelium, colorectal cancers, and pancreatic cancers.

We used the recently developed SAGE (serial analysis of gene expression) method to identify and quantify a total of 303,706 transcripts derived from human colorectal (CR) epithelium, CR cancers or pancreatic cancers (Table 1A) (3). These transcripts represented approximately 48,741

different genes (4) that ranged in average expression from 1 copy per cell to as many as 5,300 copies per cell (5). The number of different transcripts observed in each cell population varied from 14,247 to 20,471. The bulk of the mRNA mass (75%) consisted of transcripts expressed at more than five copies per cell on average (Table 1B). In contrast, the majority (86%) of transcripts were expressed at less than 5 copies per cell, but in aggregate this low abundance class represented only 25% of the mRNA mass. This distribution was consistently observed among the different samples analyzed and was consistent with previous studies of RNA abundance classes based on RNA-DNA reassociation kinetics (Rot curves). Monte Carlo simulations revealed that our analyses had a 92% probability of detecting a transcript expressed at an average of three copies per cell (7).

Table 1 - Summary of SAGE Analysis

A. Overall Summary

	Normal		Colon		Colon		Pancreatic		Pancreatic		Total
	Colon		Tumors		Cell Lines		Tumors		Cell Lines		
Total Tags	62,168		60,878		60,373		61,592		58,695		303,706
Unique Genes ¹	14,721		19,690		17,092		20,471		14,247		48,741
GenBank ²	8,753 (59)		10,490 (53)		10,193 (60)		11,547 (56)		8,922 (63)		26,339 (54)

¹ Indicates the number of different genes represented by the total tags analyzed (4).

² Indicates the number of genes that matched an entry in GenBank. The number in parentheses indicates the corresponding percentage of total unique tags.

Table 1 - Summary of SAGE Analysis

B. Summarized by Abundance Classes*

Copies/Cell	Normal		Colon		Colon		Pancreatic		Pancreatic Cell	
	Colon		Tumors		Cell Lines		Tumors		Lines	Total
> 500										
Unique Genes	62 (29)		54 (25)		54 (19)		32 (11)		70 (26)	55 (19)
GenBank	59 (95)		52 (96)		53 (98)		32 (100)		70 (100)	54 (98)
> 50 and ≤ 500										
Unique Genes	645 (28)		470 (21)		618 (27)		657 (29)		585 (27)	595 (26)
GenBank	545 (84)		429 (91)		579 (94)		609 (93)		529 (90)	553 (93)
> 5 and ≤ 50										
Unique Genes	4,569 (27)		5,011 (29)		5,733 (34)		6,146 (36)		4,895 (31)	6,209 (30)
GenBank	2,893 (63)		3,204 (64)		3,682 (64)		4,054 (66)		3,168 (65)	4,241 (68)

≤ 5						
Unique Genes	9,445 (16)	14,155 (25)	10,687 (20)	13,636 (24)	8,697 (16)	41,882 (25)
GenBank	5,256 (56)	6,805 (48)	5,879 (55)	6,852 (50)	5,155 (59)	21,491 (51)

*For unique genes, the first number denotes the number of different genes (4) represented in the indicated abundance class. The number in parentheses indicates the mass fraction (X100) of total transcripts represented by the indicated abundance class. For GenBank entries, the first number indicates the number of different genes that matched an entry in GenBank in the indicated abundance class. The number in parentheses indicates the corresponding percentage of total genes.

Many of the SAGE tags appeared to represent previously undescribed transcripts, as only 54% of the tags matched entries in GenBank (Table 1). Twenty percent of these matching transcripts corresponded to characterized mRNA sequence entries in GenBank, whereas 80% matched uncharacterized EST entries. As expected, the likelihood of a tag being present in the databases was related to abundance; GenBank matches were identified for 98% of the transcripts expressed at more than 500 copies per cell but for only 51% of the transcripts expressed at ≤ 5 copies per cell. Because the SAGE data provide a quantitative assay of transcript abundance, unaffected by differences in cloning or PCR efficiency, these data provide an independent and relatively unbiased estimate of the current completeness of publicly available EST databases.

EXAMPLE 2

This example demonstrates a comparison of the expression pattern of normal colon epithelium and primary colon cancers.

Comparison of expression patterns between normal colon epithelium and primary colon cancers revealed that the majority of transcripts were expressed at similar levels (Fig. 1A). However, the expression profiles also revealed 289 transcripts that were expressed at significantly different levels [$P < 0.01$, (8)]. Of these 289, 181 were decreased in colon tumors compared to normal colon (average decrease 10-fold; Fig. 1B; examples in Fig. 2A). Conversely, 108 transcripts were expressed at higher levels in the colon cancers than in normal colon (average increase 13-fold; Fig. 1C; examples in Fig. 2A). Monte Carlo simulations indicated that the analysis would have detected over 95% of those transcripts expressed at a 6-fold or greater level in normal vs. tumor cells or vice versa (9). Because relatively stringent criteria were used for defining differences [$P < 0.01$, (8)], the number of differences reported above is likely to be an underestimate.

EXAMPLE 3

This example demonstrates the similarities and differences between cancer cell line transcription and transcription of primary cancer tissues.

To determine how many of the 289 differences were independent of the cellular microenvironment of cancers *in vivo*, SAGE data from CR cancer cell lines was compared to that from primary CR cancer tissues (Fig. 1B, 1C). Perhaps surprisingly, the majority of transcripts (130 of 181) that were expressed at reduced levels in cancer cells *in vivo* were also expressed at significantly lower levels in the cell lines (Fig. 1B). Likewise, a significant fraction of the transcripts expressed at increased levels in primary cancers were also expressed at higher levels in the CR cancer cell lines (Fig. 1C). Thus, many of the gene expression differences that distinguish normal from tumor cells *in vivo* persist during *in vitro* growth. However, despite these similarities there were also many differences. For example, only 47 of 228 genes expressed at higher levels in CR cancer cell lines were also expressed at high levels in the primary CR cancers.

In combination, comparing the expression pattern of CR cancer cells (*in vivo* or *in vitro*) to normal colon revealed 548 differentially expressed transcripts (Fig. 1B,C, Tables 2 and 3). The average difference in expression for these transcripts was 15 fold. Although the ability to detect differences is influenced by the magnitude of the variance with the power to detect smaller differences being less, 92 transcripts that were less than three fold different were identified among the 548 transcripts. However, those genes exhibiting the greatest differences in expression are likely to be the most biologically important.

EXAMPLE 4

This example demonstrates the similarities and differences between colorectal cancer transcription and pancreatic cancer transcription.

To determine whether the changes noted in CR cancers were neoplasia or cell type specific, we performed SAGE on mRNA derived from pancreatic cancers.

A total of 404 transcripts were expressed at higher levels in pancreatic cancers compared to normal colon epithelium (examples in Fig. 2B). The majority (268) of these transcripts were pancreas-specific (10) (Example in Fig. 2C) although 136 were also expressed at high levels in CR cancers. These 136 transcripts constituted 47% of the 289 transcripts increased in CR cancers relative to normal colon and are likely to be related to the neoplastic process rather than to the specific cell type of origin.

EXAMPLE 5

This example demonstrates the reproducibility of the transcription patterns observed among a larger number of cancer samples.

One question that arose from these data is the potential heterogeneity of expression between individual tumors. The SAGE data were acquired from two examples of each tissue type (normal colon, primary CR cancer, CR cancer cell line, etc.). To examine the generality of these expression profiles, we arbitrarily selected 27 differentially expressed transcripts and evaluated them in six to twelve samples of normal colon and primary cancers by Northern blot analysis (11). In general, expression patterns were very reproducible among different samples. Of 10 genes with elevated expression in normal colon relative to CR cancers as determined by SAGE, each was detected in the normal colon samples and was expressed at considerably lower levels in tumors (examples in Fig. 2A). Similarly, most of the genes identified by SAGE as increased in CR or pancreatic cancers were confirmed to be reproducibly expressed in the majority of primary cancers examined by Northern blot (examples in Fig. 2A). It is important to note, however, that there were differences among the cancers, with a few cancers exhibiting particularly high or low levels of individual transcripts. Such differences in gene expression

undoubtedly contribute to the observed heterogeneity in biological properties of cancers derived from the same organ .

EXAMPLE 6

5 This example demonstrates the identities of some of the transcripts which were found to be differentially expressed in tumor and normal tissues. What are the identities of the differentially expressed genes? Of the 548 differentially expressed transcripts, 337 were tentatively identified through database comparisons. When tested, the great majority (93%) of these identifications proved to be legitimate (13), as expected from previous SAGE
10 analyses . Although a large number of differentially expressed genes were identified, some simple patterns did emerge. For example, genes that were expressed at higher levels in normal colon epithelium than in CR tumors were often differentiation-related. These genes included liver fatty acid binding protein , cytokeratin 20 , carbonic anhydrase , guanylin and uroguanylin ,
15 which are known to be important for the normal physiology or architecture of the colon epithelium (Table 2). On the other hand, genes that were increased in CR cancers were often related to the robust growth characteristics that these cells exhibit. For example, gene products associated with protein synthesis, including 48 ribosomal proteins, five elongation factors, and five genes
20 involved in glycolysis were observed to be elevated in both CR and pancreatic cancers compared to normal colon cells. Although the majority of the transcripts could not have been predicted to be differentially expressed in cancers, several have previously been shown to be dysregulated in neoplastic cells. The latter included IGFII , B23 nucleophosmin, the Pi form of
25 glutathione S-transferase, and several ribosomal proteins which were all increased in cancer cells as previously reported. Likewise, Dra and gelsolin were both decreased in cancer as previously reported. Surprisingly, two widely studied oncogenes, *c-fos* and *c-erbB3*, were expressed at much higher levels in normal colon epithelium than CR cancers, in contrast to their up-regulation in
30 transformed cells .

In summary, these data provide basic information necessary for understanding the gene expression differences that underlie cancer phenotypes. They additionally provide a necessary framework for interpreting the significance of individual differentially expressed genes. Although this study demonstrated that a large number of such differences exist (approximately 500 at the depth of analysis employed), it was equally remarkable that the fraction of transcripts exhibiting significant differences was relatively small, representing 1.5 % of the transcripts detected in any given cell type (26). The fact that many, but not all, of the differences were preserved during in vitro culture demonstrates the utility of cultured lines for examination of some aspects of gene expression, but also provides a note of caution in relying on such lines to perfectly mimic tumors in their natural environment. Finally, the finding that hundreds of specific genes are expressed at different levels in CR cancers, and that some of these are also expressed differentially in pancreatic cancers, provides a wealth of new reagents for future biologic and diagnostic experimentation.

REFERENCES AND NOTES

1. M. D. Adams, *et al.*, *Nature* **377**, **supp. 28**, 3 (1995); M. Schena, D. Shalon, R. W. Davis, P. O. Brown, *Science* **270**, 467 (1995); J. Derisi, *et al.*, *Nature Genetics* **14**, 457 (1996); T. M. Gress, *et al.*, *Oncogene* **13**, 1819 (1996); D. J. Lockhart, *et al.*, *Nature Biotechnology* **14**, 1675 (1996); M. Schena, *et al.*, *Proc Natl Acad Sci U S A* **93**, 10614 (1996).
2. V. E. Velculescu, L. Zhang, B. Vogelstein, K. W. Kinzler, *Science* **270**, 484 (1995); V. E. Velculescu, *et al.*, *Cell* **88**, 243 (1997).
3. To minimize individual variation, approximately equal numbers of tags (30,000) were derived from two different patients for each tissue. For primary tumors (two CR carcinomas and two pancreatic adenocarcinomas), RNA was isolated from portions of tumors judged to contain 60%-90% tumor cells by histopathology. The cells grown in vitro were derived from CR (SW837, Caco2) and pancreatic (ASPC-1, PL45) cancer cell lines. CR epithelial cells were isolated from sections of normal colon mucosa from two patients using EDTA as previously described [S. Nakamura, I. Kino, S. Baba, *Gut* **34**, 1240 (1993)]. Histopathology confirmed that the isolated cells were greater than 90% epithelial. Isolation of Poly-A RNA and SAGE was performed as previously described (2). SAGE data was analyzed by means of SAGE software and GenBank Release 95 as previously described (2).
4. A total of 69,393 different SAGE tags were identified among the 303,706 tags analyzed. A small fraction of these different tags were likely due to sequencing errors. SAGE analysis of yeast (2), wherein the entire genomic sequence is known, demonstrated a sequencing error rate of ~ 0.7%, translating to a SAGE tag error rate of 6.8% ($1 - 0.993^{10}$). Because these sequencing mistakes are essentially random, they do not substantially affect the analysis although they could artificially inflate the number of unique genes identified. Therefore, to be conservative, we reduced our estimate of unique genes identified by this maximum tag error rate (e.g., 6.8% of 303,706 total tags). The number of different tags derived from the same gene due to alternative splicing was assumed to be negligible.

5. Abundances can be simply determined by dividing the observed number of tags for a given transcript by the total number of tags obtained. An estimate of approximately 300,000 transcripts per cell was used to convert the abundances to copies per cell [N. D. Hastie, J. O. Bishop, *Cell* 9, 761 (1976)].

5 6. J. O. Bishop, J. G. Morton, M. Rosbash, M. Richardson, *Nature* 250, 199 (1974); B. Lewin, *Gene Expression Vol 2* (John Wiley and sons, New York 1980).

7. Computer simulations indicated that analysis of 300,000 tags would yield a 92 % chance of detecting a tag for a transcript whose expression was at least three copies per cell on average among the tissues examined and assuming 300,000 transcripts per cell.

8. To minimize the number of assumptions and to account for the large number of comparisons being made, Monte Carlo analysis was used for determining statistical significance. The null hypothesis was that the level, kind, and distribution of transcripts were the same for cancer and normal cells. For each transcript, 100,000 simulations were performed to determine the relative likelihood due to chance alone ("p-chance") of obtaining a difference in expression equal to or greater than the observed difference, given the null hypothesis. This likelihood was converted to an absolute probability value by simulating 40 experiments in which a representative number of transcripts (27,993 transcripts in each experiment) was identified and compared. The distribution of transcripts used for these simulations was derived from the average level of expression observed in the original samples. The distribution of the p-chance scores obtained in the 40 simulated experiments (false positives) was then compared to those obtained experimentally. Based on this comparison, a maximum value of 0.0005 was chosen for p-chance. This yielded a false positive rate that was no higher than 0.01 for the least significant p-chance value below the cutoff.

9. Two hundred simulations assuming an abundance of 0.0001 in one sample and 0.0006 in a second sample revealed a significant difference ($P < 0.01$, [8]) 95% of the time.

10. It is not possible to obtain pancreatic ductal epithelium, from which pancreatic carcinomas arise, in sufficient quantities to perform SAGE. It is therefore not possible to determine whether these transcripts were derived from genes that were highly expressed only in pancreatic cancers or were also expressed in pancreatic duct cells.

11. Total RNA isolation and Northern blot analysis was performed as described [W. S. el-Deiry, *et al.*, *Cell* 75, 817 (1993)].

12. A. H. Owens, D. S. Coffey, S. B. Baylin, Eds., *Tumor Cell Heterogeneity: Origins and Implications* (Academic Press, New York, 1982).

13. Northern blot analyses were done on 45 of the 337 differentially expressed transcripts with tentative database matches. In three cases, the pattern of expression was not differentially expressed as predicted by SAGE and, for the purposes of this calculation, were presumed to represent incorrect database matches.

14. D. C. Rubin, D. E. Ong, J. I. Gordon, *Proc Natl Acad Sci U S A* 86, 1278 (1989); K. Okubo, J. Yoshii, H. Yokouchi, M. Kameyama, K. Matsubara, *DNA Res* 1, 37 (1994).

15. R. Moll, *et al.*, *Differentiation* 53, 75 (1993).

16. J. Sowden, S. Leigh, I. Talbot, J. Delhanty, Y. Edwards, *Differentiation* 53, 67 (1993).

17. F. J. de Sauvage, *et al.*, *Proc Natl Acad Sci U S A* 89, 9089 (1992).

18. R. C. Wiegand, *et al.*, *FEBS Lett* 311, 150 (1992).

19. J. V. Tricoli, *et al.*, *Cancer Res* 46, 6169 (1986); S. Lambert, J. Vivario, J. Boniver, R. Gol-Winkler, *Int J Cancer* 46, 405 (1990).

20. W. Y. Chan, *et al.*, *Biochemistry* 28, 1033 (1989).

21. J. D. Hayes, D. J. Pulford, *Crit Rev Biochem Mol Biol* 30, 445 (1995).

22. G. F. Barnard, *et al.*, *Cancer Res* 52, 3067 (1992); P. J. Chiao, D. M. Shin, P. G. Sacks, W. K. Hong, M. A. Tainsky, *Mol Carcinog* 5, 219 (1992); N. Kondoh, C. W. Schweinfest, K. W. Henderson, T. S. Papas,

Cancer Res 52, 791 (1992); G. F. Barnard, *et al.*, *Cancer Res* 53, 4048 (1993); M. G. Denis, *et al.*, *Int J Cancer* 55, 275 (1993); J. M. Frigerio, *et al.*, *Hum Mol Genet* 4, 37 (1995).

5 23. C. W. Schweinfest, K. W. Henderson, S. Suster, N. Kondoh, T. S. Papas, *Proc Natl Acad Sci U S A* 90, 4166 (1993).

 24. M. Tanaka, *et al.*, *Cancer Res* 55, 3228 (1995); D. Medina, F. S. Kittrell, C. J. Oborn, M. Schwartz, *Cancer Res* 53, 668 (1993).

10 25. A. D. Miller, T. Curran, I. M. Verma, *Cell* 36, 51 (1984); M. H. Kraus, W. Issing, T. Miki, N. C. Popescu, S. A. Aaronson, *Proc Natl Acad Sci U S A* 86, 9193 (1989).

 26. In the case of normal and neoplastic colon cancer tissue, 548 differentially transcripts were identified among the 36,125 unique transcripts.

 27. All references cited are hereby incorporated by reference herein.

15 28. Sequences tags in Tables 2-4 are consecutively numbered to form SEQ ID NOS: 1-732.

CLAIMS

1. A method of diagnosing colon cancer in a sample suspected of being neoplastic, comprising the steps of:

5 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 3;

10 identifying the first sample as neoplastic when the level of the at least one transcript is found to be lower in the first sample than in the second sample.

2. A method of diagnosing colon cancer in a sample suspected of being neoplastic, comprising the steps of:

15 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2;

20 identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

3. The method of claim 1 wherein a comparison of at least two of said transcripts is performed.

25 4. The method of claim 2 wherein a comparison of at least two of said transcripts is performed.

5. The method of claim 1 wherein a comparison of at least five of said transcripts is performed.
6. The method of claim 2 wherein a comparison of at least five of said transcripts is performed.
- 5 7. The method of claim 1 wherein a comparison of at least ten of said transcripts is performed.
8. The method of claim 2 wherein a comparison of at least ten of said transcripts is performed.
- 10 9. The method of claim 1 wherein a comparison of at least twenty of said transcripts is performed.
- 10 10. The method of claim 2 wherein a comparison of at least twenty of said transcripts is performed.
11. The method of claim 1 wherein a comparison of at least thirty of said transcripts is performed.
- 15 12. The method of claim 2 wherein a comparison of at least thirty of said transcripts is performed.
13. An isolated and purified human nucleic acid molecule which comprises a SAGE tag selected from SEQ ID NO:1-732.
14. The nucleic acid molecule of claim 13 which is a cDNA molecule.

15. The nucleic acid molecule of claim 13 wherein the SAGE tag is located at the 3' end of the molecule, adjacent to the 3'-most NlaIII restriction enzyme site.
- 5 16. An isolated nucleotide probe comprising at least 10 nucleotides of a human nucleic acid molecule, wherein the human nucleic acid molecule comprises a SAGE tag selected from SEQ ID NO: 1-732.
17. The probe of claim 16 which comprises the selected SAGE tag.
18. A diagnostic reagent for evaluating neoplasia of a colorectal tissue, comprising at least 2 probes according to claim 16.
- 10 19. The diagnostic reagent of claim 18 which comprises at least 5 probes according to claim 16.
20. The diagnostic reagent of claim 18 which comprises at least 10 probes according to claim 16.
- 15 21. The diagnostic reagent of claim 18 which comprises at least 20 probes according to claim 16.
22. The diagnostic reagent of claim 18 which comprises at least 30 probes according to claim 16.
23. A diagnostic reagent for evaluating neoplasia of a colorectal tissue, comprising at least 2 probes according to claim 17.
- 20 24. A method of diagnosing pancreatic cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a pancreatic tissue suspected of being neoplastic and the second sample is of a normal human colon tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4;

identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

25. A method of diagnosing cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a tissue suspected of being neoplastic and the second sample is of a normal human tissue of the same tissue type, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5;

identifying the first sample as neoplastic when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

26. A method to aid in the determination of a prognosis for a colon cancer patient, comprising the steps of:

comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic colonic tissue and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 3;

determining a poorer prognosis if the level of the at least one transcript is found to be lower in the first sample than in the second sample.

27. A method to aid in determining a prognosis for a patient with colon cancer, comprising the steps of:

comparing the level of at least one transcript in a first tissue sample to a second sample, wherein the first sample is of a colonic cancer tissue and the second sample is of a normal human colonic tissue, and wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2;

determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

28. A method of diagnosing colon cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 3;

identifying the first sample as neoplastic when the level of expression of the protein is found to be lower in the first sample than in the second sample.

29. A method of diagnosing colon cancer in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a colonic tissue suspected of being neoplastic and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2;

identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

30. A method to aid in determining a prognosis of a patient having pancreatic cancer, comprising the steps of:

5 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic pancreatic tissue and the second sample is of a normal human colon tissue, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4;

 determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

10 31. A method to aid in providing a prognosis for a cancer patient, comprising the steps of:

 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic tissue and the second sample is of a normal human tissue of the same tissue type, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5;

15 determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

20 32. A method of diagnosing pancreatic cancer in a sample suspected of being neoplastic, comprising the steps of:

 comparing the level of expression of at least one protein encoded by a transcript in a first sample of a tissue to a second sample, wherein the first sample is of a pancreatic tissue suspected of being neoplastic and the second sample is of a normal human colon tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4;

25 identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

33. A method of diagnosing cancer in a sample suspected of being neoplastic, comprising the steps of:

5 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a tissue suspected of being neoplastic and the second sample is of a normal human tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5;

 identifying the first sample as neoplastic when expression of the protein is found to be higher in the first sample than in the second sample.

10 34. A method to aid in the determination of a prognosis for a colon cancer patient, comprising the steps of:

 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic colonic tissue and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 3;

15 determining a poorer prognosis if the level of expression is found to be lower in the first sample than in the second sample.

20 35. A method to aid in determining a prognosis for a patient with colon cancer, comprising the steps of:

 comparing the level of expression of at least one protein in a first tissue sample to a second sample, wherein the first sample is of a colonic cancer tissue and the second sample is of a normal human colonic tissue, and wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2;

25 determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

36. A method to aid in determining a prognosis of a patient having pancreatic cancer, comprising the steps of:

5 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic pancreatic tissue and the second sample is of a normal human colon tissue, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4;

 determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

10 37. A method to aid in providing a prognosis for a cancer patient, comprising the steps of:

 comparing the level of expression of at least one protein in a first sample of a tissue to a second sample, wherein the first sample is of a neoplastic tissue and the second sample is of a normal human tissue of the same tissue type, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5;

15 determining a poorer prognosis if the level of expression is found to be higher in the first sample than in the second sample.

38. A method of treating a cancer cell, comprising the step of:

20 administering to a cancer cell an antibody which specifically binds to a protein encoded by a transcript identified by a tag selected from the group consisting of those shown in Tables 2, 4, and 5, wherein the antibody is linked to a cytotoxic agent.

25 39. An antibody linked to a cytotoxic agent, wherein the antibody specifically binds to a protein encoded by a transcript identified by a tag selected from the group consisting of those shown in Tables 2, 4, and 5.

40. A method of detecting colon cancer in a patient, comprising the steps of:

5 comparing the level of at least one protein in a first body sample to a second body sample, wherein the first sample is a body sample of the patient and the second sample is of a normal human, wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

10 identifying neoplasia when the level of the at least one protein is found to be higher in the first sample than in the second sample.

41. A method of detecting pancreatic cancer in a patient, comprising the steps of:

15 comparing the level of at least one protein encoded by a transcript in a first sample of a tissue to a second sample, wherein the first sample is of the patient and the second sample is of a normal human, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

20 identifying neoplasia when the level of the at least one protein is found to be higher in the first sample than in the second sample.

42. A method of detecting cancer in a patient, comprising the steps of:

25 comparing the level of at least one protein in a first sample to a second sample, wherein the first sample is of patient and the second sample is of a normal human, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 5, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

identifying neoplasia when the level of the at least one protein is found to be higher in the first sample than in the second sample.

43. A method to aid in determining a prognosis for a patient with colon cancer, comprising the steps of:

5 comparing the level of at least one protein in a first sample to a second sample, wherein the first sample is of a colonic cancer patient and the second sample is of a normal human, wherein the protein is encoded by a transcript identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second sample is a sample selected from the
10 group consisting of blood, urine, feces, sputum, and serum;

 determining a poorer prognosis if the level of the at least one protein is found to be higher in the first sample than in the second sample.

44. A method to aid in determining a prognosis of a patient having pancreatic cancer, comprising the steps of:

15 comparing the level of at least one protein in a first sample to a second sample, wherein the first sample is of a pancreatic cancer patient and the second sample is of a normal human, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those shown Table 4, wherein said first and second sample is a sample selected from the
20 group consisting of blood, urine, feces, sputum, and serum;

 determining a poorer prognosis if the level of the at least one protein is found to be higher in the first sample than in the second sample.

45. A method to aid in providing a prognosis for a cancer patient, comprising the steps of:

25 comparing the level of expression of at least one protein in a first sample to a second sample, wherein the first sample is of a cancer patient and the second sample is of a normal human, wherein said protein is encoded by a transcript identified by a tag selected from the group consisting of those

shown Table 5, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one protein is found to be higher in the first sample than in the second sample.

5 46. A method of detecting colon cancer in a patient, comprising the steps of:

 comparing the level of at least one transcript in a first body sample to a second body sample, wherein the first sample is a body sample of the patient and the second sample is of a normal human, wherein the transcript
10 is identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

 identifying neoplasia when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

15 47. A method of detecting pancreatic cancer in a patient, comprising the steps of:

 comparing the level of at least one transcript in a first sample of a tissue to a second sample, wherein the first sample is of the patient and the second sample is of a normal human, wherein said transcript is identified by a
20 tag selected from the group consisting of those shown Table 4, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

 identifying neoplasia when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

25 48. A method of detecting cancer in a patient, comprising the steps of:

 comparing the level of at least one transcript in a first sample to a second sample, wherein the first sample is of patient and the second sample is of a normal human, wherein said transcript is identified by a tag selected

from the group consisting of those shown Table 5, wherein the first and second body sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

5 identifying neoplasia when the level of the at least one transcript is found to be higher in the first sample than in the second sample.

49. A method to aid in determining a prognosis for a patient with colon cancer, comprising the steps of:

10 comparing the level of at least one transcript in a first sample to a second sample, wherein the first sample is of a colonic cancer patient and the second sample is of a normal human, wherein the transcript is identified by a tag selected from the group consisting of those shown in Table 2, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

15 determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

50. A method to aid in determining a prognosis of a patient having pancreatic cancer, comprising the steps of:

20 comparing the level of at least one transcript in a first sample to a second sample, wherein the first sample is of a pancreatic cancer patient and the second sample is of a normal human, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 4, wherein said first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

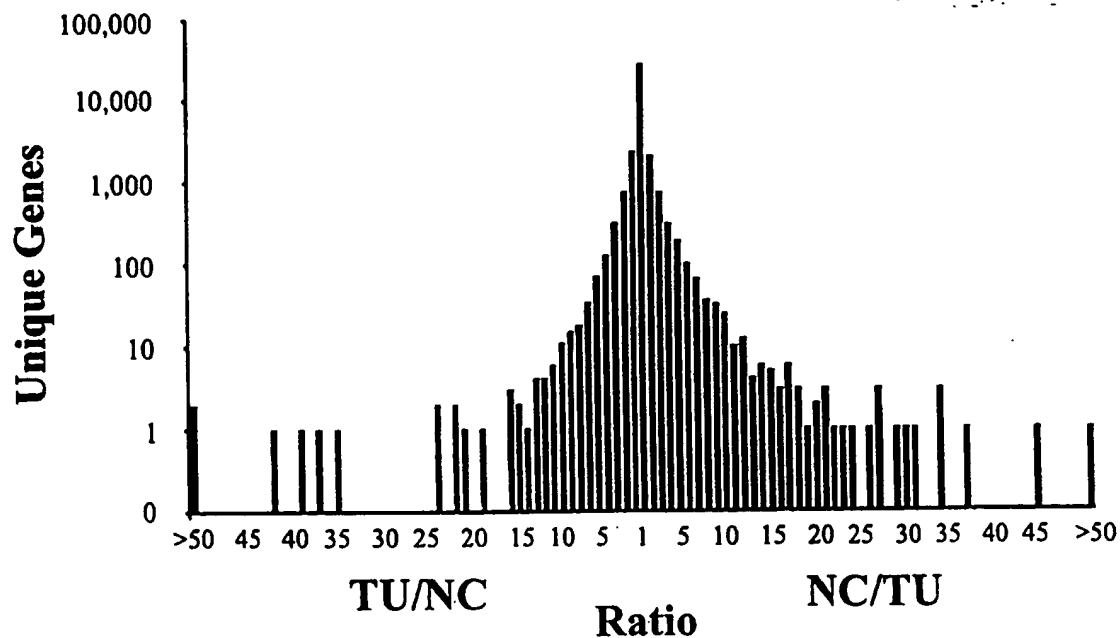
25 determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

51. A method to aid in providing a prognosis for a cancer patient, comprising the steps of:

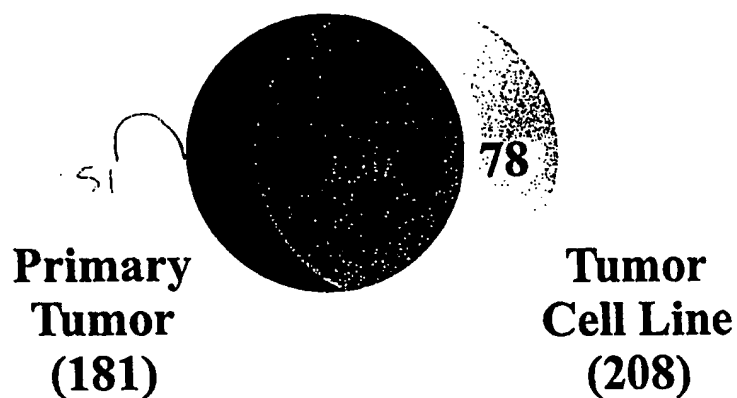
comparing the level of expression of at least one transcript in a first sample to a second sample, wherein the first sample is of a cancer patient and the second sample is of a normal human, wherein said transcript is identified by a tag selected from the group consisting of those shown Table 5, wherein the first and second sample is a sample selected from the group consisting of blood, urine, feces, sputum, and serum;

determining a poorer prognosis if the level of the at least one transcript is found to be higher in the first sample than in the second sample.

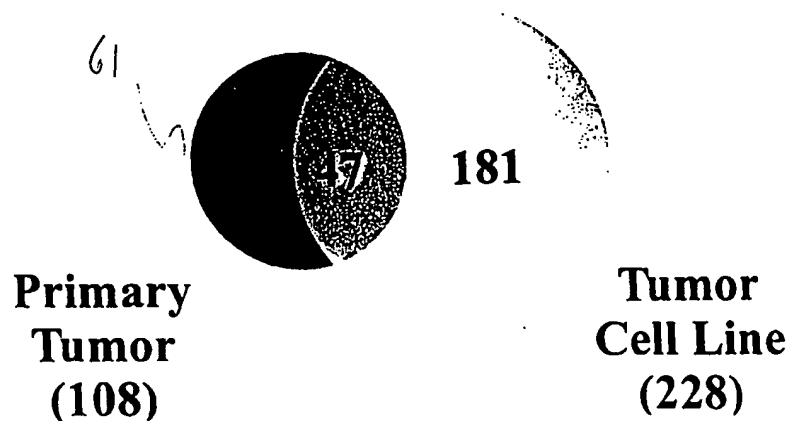
52. A method for screening for candidate agents that modulate the expression of a polynucleotide selected from the group consisting of the polynucleotides in SEQ ID NOS:1-732 or their respective complements, comprising contacting a test agent with a colon or pancreatic cell and monitoring expression of the polynucleotide, wherein the test agent which modifies the expression of the polynucleotide is a candidate agent.



B.



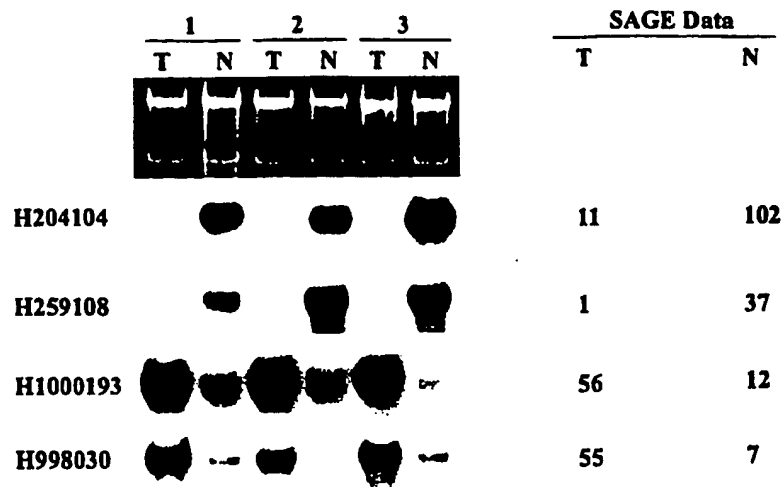
C.



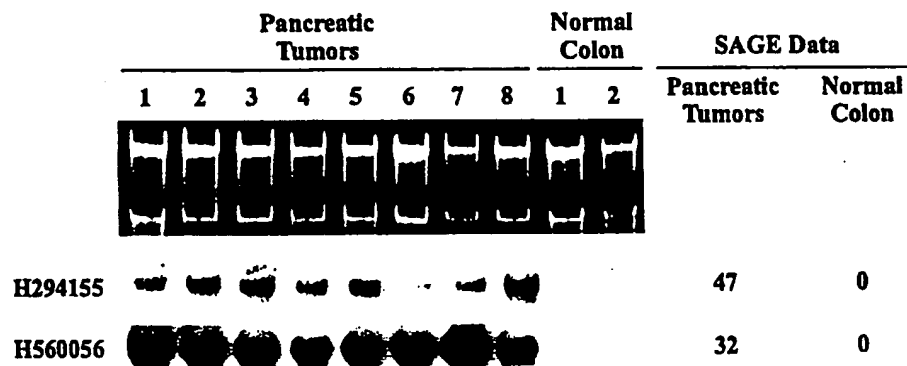
2/2

FIG. 2

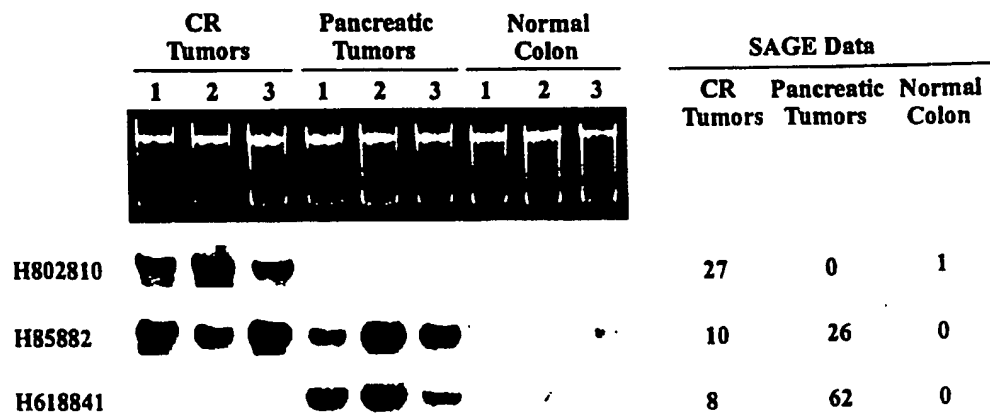
A.



B.



C.



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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12Q 1/68, G01N 33/574	A3	(11) International Publication Number: WO 98/53319 (43) International Publication Date: 26 November 1998 (26.11.98)
(21) International Application Number: PCT/US98/10277 (22) International Filing Date: 20 May 1998 (20.05.98) (30) Priority Data: 60/047,352 21 May 1997 (21.05.97) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US 60/047,352 (CON) Filed on 21 May 1997 (21.05.97) (71) Applicant (for all designated States except US): THE JOHNS HOPKINS UNIVERSITY [US/US]; Suite 2-100, 2024 E. Monument Street, Baltimore, MD 21205 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): VOGELSTEIN, Bert [US/US]; The Johns Hopkins University, Suite 2-100, 2024 E. Monument Street, Baltimore, MD 21205 (US). KINZLER, Kenneth, W. [US/US]; The Johns Hopkins University, Suite 2-100, 2024 E. Monument Street, Baltimore, MD 21205 (US).		(74) Agents: KAGAN, Sarah, A. et al.; Banner & Witcoff, Ltd., 11th floor, 1001 G Street, N.W., Washington, DC 20001-4597 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 8 July 1999 (08.07.99)
(54) Title: GENE EXPRESSION PROFILES IN NORMAL AND CANCER CELLS (57) Abstract As a step towards understanding the complex differences between normal and cancer cells, gene expression patterns were examined in gastrointestinal tumors. More than 300,000 transcripts derived from at least 45,000 different genes were analyzed. Although extensive similarity was noted between the expression profiles, more than 500 transcripts that were expressed at significantly different levels in normal and neoplastic cells were identified. These data provide insights into the extent of expression differences underlying malignancy and reveal genes that are useful as diagnostic or prognostic markers.		

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 98/10277

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12Q1/68 G01N33/574

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SUGIO K ET AL.: "Differential expression of c-myc gene and c-fos gene in premalignant and malignant tissues." CANCER RESEARCH, vol. 48, no. 17, 1988, pages 4855-4861, XP002089885 see the whole document	1,3,13, 16,17,28
X	VAN BELZEN N ET AL.: "Detection of different gene expression in differentiating colon carcinoma cells by differential display" JOURNAL OF PATHOLOGY, vol. 178, no. Suppl., - 1996 page 2A XP002089886 see abstract	1,3,5,7, 9,11
Y	---	26,28,34
	--- -/-	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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Z document member of the same patent family

Date of the actual completion of the international search

13 January 1999

Date of mailing of the international search report

24.05.1999

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 98/10277

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 95 21944 A (SMITHKLINE BEECHAM CORP ;ROSENBERG MARTIN (US); DEBOUCK CHRISTINE) 17 August 1995 see the whole document ---	26,28,34
Y	EP 0 284 362 A (ICI PLC) 28 September 1988 see abstract see page 2, line 44 - line 51 see page 10, line 12 - line 15; claims 1,9; figure 2 ---	1,3,5,7, 9,11, 13-23, 26,28, 34,52
Y	EP 0 761 822 A (UNIV JOHNS HOPKINS MED) 12 March 1997 see the whole document ---	1,3,5,7, 9,11, 13-23, 26,28, 34,52
Y	WO 95 11923 A (DANA FARBER CANCER INST INC ;CHEN LAN BO (US); BAO SHIDENG (CN); L) 4 May 1995 see the whole document ---	1,3,5,7, 9,11, 13-18, 23,26, 28,34,52
Y	VELCULESCU V E ET AL: "SERIAL ANALYSIS OF GENE EXPRESSION" SCIENCE, vol. 270, 20 October 1995, pages 484-487, XP002053721 cited in the application see the whole document ---	1,3,5,7, 9,11, 13-18, 23,26, 28,34,52
Y	SCHWEINFEST C W ET AL.: "Subtraction hybridization cDNA libraries from colon carcinoma and hepatic cancer" GENETIC ANALYSIS TECHNIQUES AND APPLICATIONS, vol. 7, 1990, pages 64-70, XP002089887 see the whole document ---	1,3,5,7, 9,11, 13-18, 23,26
Y	WO 97 14812 A (CHIRON CORP) 24 April 1997 see the whole document ---	52
A	GRESS T M ET AL.: "A pancreatic cancer-specific expression profile" ONCOGENE, vol. 13, 1996, pages 1819-1830, XP002089888 see the whole document ---	

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/10277

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 95 19369 A (UNIV VANDERBILT) 20 July 1995 see the whole document ---	
A	GRESS T ET AL.: "Identification of genes with pancreatic cancer specific expression by use of cDNA representational difference analysis" GASTROENTEROLOGY, vol. 110, no. 4 Suppl., 1996, XP002089889 see abstract ---	
P,X	ZHANG L E AL.: "Gene expression profiles in normal and cancer cells." SCIENCE, vol. 276, 1997, pages 1268-1272, XP002089890 see the whole document ---	1,3,5,7, 9,11, 13-23, 26,28, 34,52
P,X	VAN BELZEN N ET AL.: "A novel gene which is up-regulated during colon epithelial cell differentiation and down-regulated in colorectal neoplasms" LABORATORY INVESTIGATION, vol. 77, no. 1, 1997, pages 85-92, XP002089891 see the whole document -----	1,3,5,7, 9,11,13, 14, 16-18, 23,26, 28,34

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/ 10277

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see FURTHER INFORMATION sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see FURTHER INFORMATION sheet, subject 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US 98/10277

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1,3,5,7,9,11,13-23,26,28,34,52 (partial)

INVENTION 1:

An isolated and purified human nucleic acid molecule comprising SEQ ID NO:291 of table 3 (INVENTION 1), an isolated nucleotide probe hybridizing to it, a diagnostic reagent comprising at least two of such probes, methods of diagnosing or prognosing colon cancer using them, and a method for screening for agents modulating the expression of such a sequence using them.

2. Claims: 1,3,5,7,9,11,13-23,26,28,34,52 (partial)

INVENTION 2 to INVENTION 259:

An isolated and purified human nucleic acid molecule comprising SEQ ID NO:292 of table 3 (INVENTION 2), an isolated nucleotide probe hybridizing to it, a diagnostic reagent comprising at least two of such probes, methods of diagnosing or prognosing colon cancer using them, and a method for screening for agents modulating the expression of such a sequence using them.

...ibidem for each of the SEQ ID Nos:293 to 549 (INVENTION 3 to INVENTION 259) as specified in table 3, separately.

3. Claims: 2,4,6,8,10,12-23,27,29,35,38-40,43,46,49, 52 (partial)

INVENTION 260 to INVENTION 549:

An isolated and purified human nucleic acid molecule comprising SEQ ID NO:1 of table 2 (INVENTION 260), an isolated nucleotide probe hybridizing to it, a diagnostic reagent comprising at least two of such probes, methods of diagnosing or prognosing colon cancer using them, a method of treating a cancer cell using them, an antibody linked to a cytotoxic agent used in such a method, and a method for screening for agents modulating the expression of such a sequence using them.

...ibidem for each of the SEQ ID Nos:2 to 290 (INVENTION 261 to INVENTION 549) as specified in table 2, separately.

4. Claims: 13-24,30,32,36,38,39,41,44,47,50,52 (partial)

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US 98/10277

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

INVENTION 550 to INVENTION 732:

An isolated and purified human nucleic acid molecule comprising SEQ ID NO:550 of table 4 (INVENTION 550), an isolated nucleotide probe hybridizing to it, a diagnostic reagent comprising at least two of such probes, methods of diagnosing or prognosing pancreatic cancer using them, a method of treating a cancer cell using them, an antibody linked to a cytotoxic agent used in such a method, and a method for screening for agents modulating the expression of such a sequence using them.

...ibidem for each of the SEQ ID Nos:551 to 732 (INVENTION 551 to INVENTION 732) as specified in table 4, separately.

5. Claims: 24,30,32,36,38,39,41,44,47,50 (partial)

INVENTION 733 to INVENTION 734:

Methods of diagnosing or prognosing pancreatic cancer relying on a human nucleic acid molecule comprising SEQ ID NO:733 of table 4 (INVENTION 733), a method of treating a cancer cell using it, and an antibody linked to a cytotoxic agent used in such a method.

...ibidem for SEQ ID Nos:734 (INVENTION 734) as specified in table 4.

6. Claims: 25,31,33,37-39,42,45,48,51 (partial)

INVENTION 735 to INVENTION 870:

Methods of diagnosing or prognosing cancer relying on a human nucleic acid molecule comprising SEQ ID NO:735 of table 5 (INVENTION 735), a method of treating a cancer cell using it, and an antibody linked to a cytotoxic agent used in such a method.

...ibidem for each of the SEQ ID Nos:736 to 870 (INVENTION 736 to INVENTION 870) as specified in table 5, separately.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/10277

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9521944 A	17-08-1995	EP 0743989 A JP 9508800 T	27-11-1996 09-09-1997
EP 0284362 A	28-09-1988	AU 625169 B AU 1337888 A DK 159788 A FI 881388 A JP 1034291 A PT 87055 A,B	02-07-1992 22-09-1988 24-09-1988 24-09-1988 03-02-1989 01-04-1988
EP 0761822 A	12-03-1997	US 5695937 A US 5866330 A AU 6561496 A AU 7018896 A CA 2185379 A GB 2305241 A IE 80465 B JP 10511002 T WO 9710363 A	09-12-1997 02-02-1999 20-03-1997 01-04-1997 13-03-1997 02-04-1997 12-08-1998 27-10-1998 20-03-1999
WO 9511923 A	04-05-1995	CA 2175380 A EP 0725799 A US 5889159 A US 5872235 A	04-05-1995 14-08-1996 30-03-1999 16-02-1999
WO 9714812 A	24-04-1997	AU 7264196 A EP 0862651 A	07-05-1997 09-09-1998
WO 9519369 A	20-07-1995	US 5677125 A AU 1831795 A CA 2210396 A EP 0804453 A	14-10-1997 01-08-1995 20-07-1995 05-11-1997